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* Major Russell, Journal American Medical Association, August 30, 1913.

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JULY, 1915

ORIGINAL ARTICLES

PARTIAL RESECTION OF THE LOWER JAW FOR CANCER.[1]

By Edward M. Foote, M.D.,

VISITING SURGEON TO THE NEW YORK SKIN AND CANCER HOSPITAL; CLINICAL PROFESSOR OF SURGERY NEW YORK POLYCLINIC MEDICAL SCHOOL.

If an operation is only occasionally performed the exact field of its usefulness and the finer points in its technique are more or less forgotten. It is worth while to review such operations from time to time in order to examine their classical descriptions in the light of the present-day practice of surgery. Such an operation is the partial excision of the lower jaw.

This operation is rarely required for trauma, and in cases of osteomyelitis the removal of bone is almost invariably subperiosteal and not, therefore, a true resection of the jaw. It is in the presence of tumors, and especially malignant tumors, that resection of the lower jaw finds its chief use.

I have performed this operation upon fourteen patients in the last three years, and their histories form the basis of a profitable study.

The operation is almost exactly one hundred years old, having been performed for the removal of a new growth by Dupuytren in 1812. Mott, of New York, performed it in 1821, and in February, 1831, Barton published an article in the Amer. Jour. Med. Sci., in which he says: "The records of medicine in this country, as well as in Europe, have already afforded so many examples of the suc-

[1] Read before the Clinical Society of the New York Polyclinic Hospital, April 5, 1915.

cessful removal of large portions of the lower jaw, in cases where the bone had been involved in disease, as to justify and establish the practice in desperate cases, and to require that the operation should henceforth be ranked among those in regular surgery."

He illustrated his article by steel engravings of a patient before and after operation, and pictured the saw employed to divide the bone, the instrument being of a type perfectly adapted to the purpose (Fig. 1).

The early operators had as subjects for their skill, patients entirely conscious or partly stupefied with drugs, for anesthetics did not come into practical use much before 1850. The patient was seated in a strong chair and held by main force, although the polite term employed in the description is, "his head was supported by an assistant." The operation was often interrupted by the "restlessness of the patient." The ordeal must have been a severe one for all concerned. It is true that the surgeon was never hampered by an inefficient anesthetist, but that he had other troubles may be seen from O'Shaughnessy's description of an operation performed about 1821.

"Professor Lallemand, of Montpellier, removed a considerable portion of the base of the lower jaw, and when the muscles of the

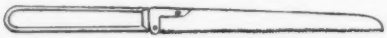

FIG. 1.—Drawing of saw used in 1831 for resection of the lower jaw. (Barton.)

tongue were cut through the patient fell senseless on the floor. The assistants and spectators rushed horror-stricken from the room. The wound was bleeding violently and the greatest consternation and dismay prevailed. The professor immediately applied the actual cautery at a white heat to the surface of the wound, which succeeded in arresting the hemorrhage. He then made an opening into the larynx between the thyroid and cricoid cartilages, through which the air rushed into the trachea, and the patient revived immediately, and ultimately perfectly recovered."

The operation as first performed was commenced by ligation of the common carotid artery, in order to control hemorrhage; but it was soon discovered that this was an unreliable procedure for the purpose and added much to the danger of the operation. It was therefore abandoned about 1820.

From such accounts of operations in the first third of the nineteenth century as I have been able to find, the incision employed ran downward from the mouth to the chin and outward along the base of the jaw. One or more teeth were extracted, sometimes a day or two previous to the operation; though one writer objected to this on the ground that the patient would be less sensible of the pain of their extraction if it were merged in the greater pains of the

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operation. After the bone was bared in the places selected for its division it was sawed part way through with a small hand saw, or a chain saw; and then its denser portion was divided with cutting forceps.

The incision practised by Cusack, in 1827, is shown in Fig. 2. It would seem that such an extensive incision must surely have produced paralysis of the mouth and lower eyelid, although no mention of this is made in the description of the cases.

Cusack preferred the chain saw, as he found it difficult to protect the soft parts while using a small hand saw, and, moreover, he was often interrupted by the "restlessness of the patient."

A *B*

FIG. 2.—*A*, large tumor of lower jaw; *B*, patient after recovery, showing line of incision. (Cusack.)

In Liston's *Practical Surgery*, published in 1837, the incision recommended passed from the condyloid process downward to the angle of the jaw and then forward to the point of the chin. It was then mentioned that to cut through the lip adds to the facial disfigurement, and is in many cases quite unnecessary.

By the latter half of the nineteenth century the operation was so far perfected that the instruments and technique described by Gerich,[2] in 1864, vary little from those employed today. At that time, however, the sitting posture was still advocated to keep the blood out of the throat of the chloroformed patient.

Up to that time a number of incisions had been practised for

[2] Ueber Resection des Unterkeifers, Dorpat, 1864.

removal of different parts of the jaw, but the advantages of curved incisions following the lower and, if necessary, posterior margins of the bone were well recognized. Gerich was also keenly alive to the desirability of protecting Steno's duct and as many branches of the facial nerve as possible.

He pointed out correctly that if an incision along the posterior border of the ascending ramus extends above the level of the lobe of the ear the dissection must be conducted with great care or the branches to the eyelids will suffer; but through an incision no more extensive than this, disarticulation of the bone has often been carried out.

There are three ways, more or less distinct, in which partial resection of the lower jaw may be performed. These are: (1) resection from within the mouth; (2) external resection without disarticulation; (3) external resection with disarticulation.

While all operations for malignant tumors have to be modified to suit the particular case, and partial resection of the lower jaw is no exception to this rule, it is none the less convenient to consider it in these three forms, and to point out under what circumstances each should be employed.

1. Resection performed wholly within the mouth is not suitable for a tumor of the jaw of greater malignancy than an epulis, unless the tumor is a primary one in an early stage, and not involving the bone.

This was the operation performed in three of the cases reported in connection with this paper (Cases II, IX, and XIV). In two of these the tumor was an epulis, and the results of operation were satisfactory even though one tumor was recurrent. In the third the tumor was recurrent and of some degree of malignancy, but, owing partly to a doubtful pathological report, a decision was made to operate within the mouth in defiance of the rule above stated. The continuance of symptoms necessitated subsequent external resection, but the most favorable time for this had then passed.

The technique of resection within the mouth is very simple. An incision is made through healthy tissue completely around the tumor, everywhere down to the bone. With a small chisel and mallet a wedge-shaped piece of bone is chiseled free and removed with the tumor. The gross specimen is examined, and if the tumor is found to involve the bone, or if the cut surface of the bone appears diseased, a deeper layer of bone should be chiseled or gauged away. Nearly the whole thickness of the jaw can be removed without disfigurement or serious permanent injury. In a doubtful case an external resection is usually to be preferred.

Hemorrhage may be controlled with gauze packing. This should be removed daily, as it quickly becomes foul. As soon as granulations are well started no further dressing is needed.

2. External resection without disarticulation of the lower jaw is indicated in all cases of malignant tumors of the jaw itself or of the mucous membrane, or other soft parts close to it, in which there is a fair prospect that the incisions will lie outside of the diseased area. As stated above a resection from within the mouth is permissible for an early epithelioma involving the mucous membrane only.

External resection without disarticulation is more readily performed than resection with disarticulation. It is less dangerous than the latter, and it carries with it less risk of injury to the upper branches of the facial nerve. It is therefore to be chosen for both radical and palliative operations in which the tumor is so situated that the ascending ramus, and the adjacent soft parts are free from disease. Particular attention should be directed to the examination of the parts inside of the mouth, for the region of the pterygoid muscles is a favorite one for extension of a growth situated as far back as the molar teeth. If the disease is in the vicinity of the ascending ramus, disarticulation should be the invariable rule. This is true of even a palliative operation, as the patient will have less pain if the upper part of the jaw is removed.

External resection, in my judgment, is not a good palliative procedure if the disease is so situated that the whole chin would have to be removed; or if as much as one-half of the floor of the mouth is involved, because in such cases the patient is usually more uncomfortable after operation than he was before it. If there is a fair chance of complete removal of the tumor, even these extensive operations may be justifiable; but a most careful examination should be made before they are decided upon. The condition of the floor of the mouth is of the greatest importance in this decision.

The technique of external resection in a simple case is as follows: An incision is made from the point of the chin along the lower margin of the jaw to the angle, and then downward along the sternomastoid muscle to its middle. Skin, fat, and platysma are cut through, the flap dissected downward, the facial artery and vein ligated and divided. The fat, facia, and glands lying between the anterior belly of the digastric muscle and the sternomastoid muscle are dissected free from the hyoid bone upward, and necessary vessels are ligated and divided. The presence of enlarged lymph glands may make necessary a dissection back of the sternomastoid, or as far down as the clavicle. This part of the operation should always be thoroughly done.

If the skin of the cheek is plainly not involved it is dissected upward for an inch or more, care being taken not to injure the upper fibers of the facial nerve. Within the mouth an incision is made wide of the tumor both along the cheek and the floor of the mouth. The external and internal wounds are deepened until

they meet on both sides of the jaw, at least at the places at which the bone is to be divided. The cheek can then be retracted upward out of the way of the saw. Any tooth which is in line of an incision through the bone should be extracted, as should be any tooth which will remain close to the incision, for a tooth so situated will become loose and give the patient much annoyance.

One of the best saws for cutting the bone is a small hack saw (Fig. 3). If an instrument maker gets hold of it he is likely to nickel plate it, thereby changing it from a real tool into an ornament. As furnished by the manufacturer it is ready to cut metal, and it cuts the "hardest bone in the body" as an ordinary saw cuts wood.

If the cheek is retracted and a strip of metal like a tongue depressor or a flat blunt scissors is held back of the bone to protect the tongue, the surgeon can work the saw vigorously in short strokes that rapidly eat away the bone. When the bone has been divided the fragment to be removed is held with strong forceps while the

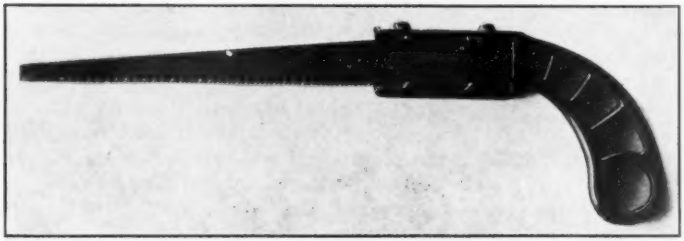


FIG. 3.—Hack saw for cutting jaw bone.

bone is sawed in the second place. If a splinter breaks off or the soft parts get in the way the section may be completed with bone shears. The loosened fragment is then turned down and its deep attachments are divided, permitting it to be removed with the mass of glands.

All bleeding is stopped by clamps or hot compresses, for as in all serious operations for malignant tumors the preservation of his blood is the salvation of the patient. Vessels which still bleed are ligated with fine catgut. The wound is carefully gone over. Suspicious spots, whether of bone or soft tissue, are still further excised. The cut ends of the bone are rounded a little with bone shears. Flaps are approximated and sutured both within the mouth and externally, except for about an inch where gauze or rubber tissue drainage is employed. It is desirable to suture the wound in the mouth completely. When this is done primary union often results throughout its greater portion and leakage is slight. If extensive removal of mucous membrane prevents complete

suture the internal wound should still be closed as nearly as possible and the remaining gap stopped with the gauze.

Primary union of so much of the external wound as is sutured is the rule, and all stitches should be removed in less than a week. The power of growth of these tissues is tremendous, and even a considerable hole into the mouth rapidly fills in.

Probably for this reason necrosis of the cut ends of the bone is not common. I experienced it only twice after nine external resections without disarticulation (eighteen cut surfaces of bone).

If the growth is so situated that the part of the jaw carrying the incisors must be removed the incision and dissection of the neck as above described should be carried out on both sides to provide for the removal of involved lymph glands.

The chief dangers of this operation are associated with (*a*) anesthesia, (*b*) excessive hemorrhage, (*c*) blood in the throat, and (*d*) falling backward of the tongue when its attachments are severed. These are all real dangers and deserve careful consideration.

(*a*) The ordinary mouth anesthesia is not well adapted to external resection of the jaw, and it adds materially to the risk of operation. Vapor anesthesia through the nose is much better if the patient can be kept under by this method, which is by no means certain. Rectal anesthesia[3] is ideal. If necessary the mask and a little ether or chloroform can be used to put the patient deeply under at the start. After that the anesthetist and his apparatus are entirely out of the way and, more important still, there is no increased mucous and saliva in the patient's throat.

(*b*) Excessive hemorrhage should be guarded against from the beginning of operation. Large vessels should be clamped before they are cut. Smaller ones should be promptly controlled by clamps or pressure. The worst region is below or back of the angle of the jaw, where a large vein may be cut laterally or some branch severed while the tissues are on the stretch. Then when they are relaxed the vein withdraws and a fountain of dark blood wells up from some unseen opening. Pressure on both sides of it to stop the flow, and division of the superficial tissues until the vessel is clearly exposed are the surest ways to meet the difficulty. It is well not to push the deep dissection in this region until the jaw has been cut through twice. The dissection can then be carried from above downward, which lessens the risk of serious venous hemorrhage, and the mobility of the bone makes deep exposure easier.

(*c*) Blood can be kept out of the throat by a good-sized pad of gauze kept in the mouth and changed as often as it becomes saturated. A string through it is a safeguard against swallowing, but

[3] Ether, 1 ounce by measure to 25 pounds of the body weight, is mixed with paraffin oil in the proportion of two parts of ether to one part of oil. This is injected slowly into the empty rectum one-half hour before operation. A preliminary hypodermic of ⅛ or ¼ grain of morphin is advisable.

a quicker way is to clamp a corner of it projecting from the mouth.

(*d*) A heavy thread should always be passed through the tongue either in the middle line or a little to the affected side. It serves to draw the tongue out of the way, and can be used to prevent the loosened tongue from blocking the throat. This accident is more likely to happen the farther forward the excision. If the digastric and muscles anterior to it are divided, the tongue sometimes almost snaps back into the throat. If held forward for a few minutes the tendency grows less as the remaining muscles become accustomed to the change; but such a patient must be watched every minute until he is well out of his anesthetic. I nearly lost one patient from suffocation produced in this way. At the close of operation I left the house surgeon to apply the dressing and went into an adjoining room. In a few minutes I was called back and found the patient black, making no effort to breathe, and almost pulseless. When the bandage was cut off and the tongue pulled forward he still made no effort to breathe, but revived after a few minutes of artificial respiration. One may readily arrange a mechanical contrivance to hold the tongue forward, but it is safer not to leave a patient for a few hours, whose tongue tends to sag back into the throat. During this time the thread should of course remain in the tongue.

3. External resection of the lower jaw with disarticulation is indicated in cases of malignant tumors situated far back in the cheek, or in the jaw bone, and especially if such a tumor is recurrent, for in such a case the involvement of the ascending ramus or of the muscles lying on its inner side may be present to an extent not readily determined by examination of the patient. The technique of its performance is similar to that of external resection. It is therefore only necessary to mention certain differences.

The incision has generally to be extended up in front of the ear a variable distance. It is quite easy to remove a normal jaw without injury to the upper branches of the facial nerve, but a wide excision of soft parts is more important than the preservation of the parotid gland and facial nerve if the tumor involves the ascending ramus or tissues in its neighborhood. Therefore, one should not hesitate to sacrifice these important structures if it seems indicated to gain an increased freedom from recurrence. If the decision is to preserve the parotid gland or the greater part of it the skin incision should not extend above the external auditory meatus and the deeper incision not quite up to this. By dissecting under the parotid, especially in its anterior portion, it will then be possible to lift it and the cheek up and out of the way so as to permit of the disarticulation of the jaw. Before this is attempted the bone should be sawed through anteriorly and the dissection within the mouth completed. The muscles are then divided along

the malar bone from in front backward. When the temporal muscle is cut from the condyloid process the fragment of the jaw can be swung outward so as to expose the joint. The rather loose capsule is cut or torn and the bone with the tumor and the attached soft parts are removed. Removal of a part of the parotid gland usually leaves the patient with an external salivary fistula, but this soon dries up if the main duct is not interfered with.

After Treatment. A patient upon whom there has been performed an external partial resection of the lower jaw, with or without disarticulation, should be carefully watched for a few hours to guard against recurrent hemorrhage or a blocking of the throat by the loosened tongue. Some of the patients have great difficulty in swallowing, especially if the dissection has been extended to the anterior pillar of the fauces. This is not to be wondered at when one thinks of the extent of the wound and its close relation to the muscles of tongue and throat.

No nourishment should be put into the patient's mouth until he has shown his ability to swallow water. In severe cases it may be necessary to employ nutrient enemata for a few days or, preferably, to pour fluids through a slender stomach tube passed through the nose and into the esophagus. It is not necessary for the tube to reach the stomach, so that a large rubber catheter may be used if no small stomach tube is at hand. This should be done only twice or three times a day, and a pint or more of water and fluid nourishment poured slowly through it each time.

Most patients swallow readily after two or three days. Only one patient in the present series (Case XI) had a prolonged difficulty in swallowing, and his tumor was so extensive that a part of his pharynx was cut out.

It is a good plan to allow these patients to sit up as soon as they may desire, sometimes after three or four days. They quickly learn to keep the mouth rinsed out, especially after taking nourishment, and if fluids from the mouth render the dressings foul, these should be changed twice daily. Postoperative pain is not as great as one might suppose from the extent of operation. The discomfort of the patient seems to be less than that which follows an excision of the tongue.

Results of Operation. Soon after operation the portion of the lower jaw which remains swings toward the operated side, thus bringing the molars within those of the upper jaw and the incisors back of the upper incisors. Various plans have been suggested to prevent this, two of which are worth mentioning: The upper and lower teeth may be wired together for a few weeks to keep the lower jaw in place while the wound is healing. A prothesis of wire or rubber, or some other non-irritating material, or a strip of live bone, may be inserted between the fragments of the bone after resection without disarticulation.

I have never employed these devices in malignant cases, as I believe their use is not advisable. Wiring the jaws is a dirty and irritating procedure, and the patient needs all the help he can have to keep his mouth in good condition. The use of a foreign body between the fragments is also a source of irritation under circumstances in which an absolute primary union can scarcely be hoped for. Moreover, the possibility of recurrence is so great that the patient must be watched from month to month, and another operation performed as soon as the tumor shows itself in any part. If a foreign body is present to change the appearance of the wound by its own irritation the early recognition of the new tumor formation is rendered more difficult; and if a second operation proves necessary, the prothesis must, of course, be removed.

It has been suggested to insert a prothesis at a late period, but it is difficult to do this satisfactorily even a year after operation; and a much longer time than that must elapse before one can feel sure that there will be no recurrence. Moreover, in many cases there has been so wide a removal of the soft parts, that only a scar remains in which to bury the prothesis. In other words, the conditions are very different from those which follow the loss of a portion of the horizontal ramus by trauma or inflammation, and in which there has been very little loss of the soft parts.

The decision to reject all foreign bodies in the month after these operations is confirmed by the good functional results which have followed operation in this series of cases, provided the patient has been freed of his malignant disease. Every such patient has good motion of the jaw, and most of them have so developed the lateral motion as to be able to chew on the sound side. One man even goes so far as to claim the operation has cured a long-standing dyspepsia, since now he has to eat more slowly.

Photographs of five of these patients are introduced to show the amount of disfigurement which results from operation and the functional power of the jaw and eyelids.

Late Results. The late results can best be estimated when considered in connection with the character and situation of the growth.

All but one of the fourteen patients operated upon were men.

The ages varied from thirty to seventy-five years, more than half of the patients being between forty-five and fifty-five years old.

As nearly as one could judge the growth started in the jaw (usually in its mucous membrane) in 8 cases; in the lining of the cheek in 3 cases; in the angle of the mouth in 2 cases; while the spindle-cell sarcoma in Case VII seemed to start just below the jaw, possibly from its periosteum.

Nine of the patients had recurrent tumors following operation elsewhere when they first came under my observation. Two presented themselves with primary tumors of the cheek, which I excised

without resection. In both of these cases subsequent removal of the bone failed to arrest the growth. In 3 cases resection was the first operation performed, and in these patients no recurrence has showed itself. It is impossible to state positively that a primary resection would have saved the others, but it would certainly have given them a better chance. If anyone thinks that primary resection is unnecessarily mutilating it is only necessary to point out how rapidly a tumor of the cheek can spread in spite of lesser operations, as seen in Cases X and XII.

Of the eleven resections performed for recurrences, four were known to be merely palliative, but even in these cases the operation seemed well worth while, as the patient was given a clean mouth for varying periods of time. Ten resections were performed with the hope of a permanent cure, 3 being primary operations and 7 after recurrences from other operations. One of these patients died from operation and 2 others from recurrences, while the remaining 7 are at present free from recurrence as far as physical examination can show after periods ranging from six to thirty-three months. It is probably too much to expect that all of these patients are cured, but I think we are justified in saying that the prognosis following partial resection of the lower jaw for cancer is more hopeful than it is generally supposed to be.

A summary of these cases is presented on page 24.

Case I.—Male, aged seventy-five years. Disease noticed in the right side of the lower jaw for one and a half years. Operation from within the mouth in Richmond, Va. Recurrence soon appeared, but further operating was discouraged.

Operation at New York Skin and Cancer Hospital April 9, 1912. Resection of two and a half inches of the right side of the lower jaw by incisions within the mouth and below the jaw. The anterior cut near the median line showed the remaining bone to be diseased. The posterior cut was through apparently healthy bone. On account of the age and feeble condition of the patient a more extensive operation was considered inadvisable. The wound in the mouth was entirely sutured, as was the skin wound. Primary union resulted with a minute sinus leading to the anterior cut in the bone.

The patient did well for some weeks; then noticing the recurrence, he consulted another surgeon in Richmond, who removed the chin and part of the left ramus. Patient died from shock in forty-eight hours.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

Case II.—Female, aged forty-five years. Ten months disease existed as a small nodule on the lower jaw opposite the second right bicuspid. After seven months this was removed, with two bicuspid teeth and one molar. In two months recurrence was noticed of a hard, purplish color, with ulceration, at times painful.

Operation at New York Skin and Cancer Hospital July 2, 1912. Right incisors, canine, and second molar teeth were removed. The tumor with surrounding mucous membrane was excised, half or more of the thickness of the jaw bone in its vicinity being chiseled away. The remaining mucous membrane was sutured. The patient recovered promptly.

Two years and nine months later the patient was examined and found free from recurrence.

Pathological diagnosis by Dr. Jessup: epulis, giant-cell sarcoma type. Bone not invaded.

CASE III.—Male, aged forty-four years. Growth began as a blister in the right angle of the mouth. Patient was operated upon in ten days at the Long Branch Hospital, and operated upon a second time one year later. There was again a recurrence, with rapid growth. Fifteen months after the tumor was first noticed it extended from the right angle of the jaw to the median line and from the lip to one inch below the lower margin of the jaw.

Operation at New York Skin and Cancer Hospital August 1, 1912. Most of the patient's lower lip, his chin, and a portion of the lower jaw measuring two and three-quarter inches, mostly on the right side, were removed, together with the submaxillary gland and enlarged lymph glands. The flaps were undermined and an incision to relieve tension was made through the skin of the right cheek. This permitted a complete suture. Gap in the cheek covered with skin grafts. Wound healed primarily, the skin grafts all taking. Patient discharged in eleven days.

Operation at New York Skin and Cancer Hospital September 24, 1912, for a recurrence in the right cheek about three-quarters of an inch in diameter. Wound healed primarily. One month later patient wrote that his face was smooth and all healed. Five months later recurrence began to trouble him and ten and a half months after resection of his jaw, he died.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

CASE IV.—Male, aged fifty-four years. The tumor began in the inner side of the right cheek opposite the second molar. In one year it reached the diameter of about one inch and extended close to the lower jaw.

Operation at New York Skin and Cancer Hospital August 27, 1912. An incision was made across the neck below the jaw and curving upward in front of the ear, also for a short distance down the sternomastoid. The cheek was divided around the tumor. The jaw was cut through back of the bicuspid teeth, twisted out of its articulation, and removed with the tumor and the submaxillary and parotid glands. Branches of the facial nerve to the mouth and eye were divided. Patient was a good deal shocked but recovered sufficiently to leave the hospital in three weeks. Sagging of the

lower eyelid gradually became less marked. Two years and eight months after operation there were no signs of recurrence and patient was in good health (Fig. 4).

Front view, mouth and eyes closed.

Side view, mouth and eyes closed.

Front view, mouth and eyes open.

Side view, mouth and eyes open.

FIG. 4.—Patient No. IV, twenty-nine months after partial resection of the lower jaw, with diarticulation, for epithelioma of cheek. Partial paralysis of the mouth and the right eyelids has gradually lessened until the lips open and close almost normally and the conjunctivitis has disappeared.

Pathological diagnosis by Dr. Jessup: epithelioma of the cheek; no invasion of the lower jaw or lymph nodes.

CASE V.—Male, aged thirty-four years. A tumor began in the left angle of the mouth and in six months reached the size of the end of a thumb, when a V-shaped portion was excised from the lower lip at Red Bank, N. J. Five months later a mass about one inch in diameter was removed from the lower jaw at Asbury Park, N. J. Three months later another small mass was removed by another surgeon. Recurrence persisted until it involved the left horizontal ramus of the jaw and most of the cheek.

Operation at New York Skin and Cancer Hospital October 10, 1912. An incision was made from the left angle of the mouth backward to the angle of the jaw and a second incision carried backward below the horizontal portion of the jaw. The jaw was cut through at the symphysis and behind the angle. A portion of the cheek between these incisions, the part of the lower jaw indicated, and the glands of the submaxillary region and below the angle of the jaw were removed. The wounds in the mucous membrane and the skin were entirely sutured and healed primarily, except at drain points. The patient did well for some months and died of recurrence nine months after operation.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

CASE VI.—Male, aged fifty-two years. Noticed a tender mass under right side of the lower jaw after doing some heavy lifting. Six months later an enlarged "gland" was removed by his physician. Subsequent growth was rapid, with discharge of pus and blood. One month later a mass three inches in diameter involved the right horizontal portion of the lower jaw.

Operation at St. Mary's Hospital, Jamaica, L. I., June 20, 1913. An elliptical incision was made around the tumor and extended down the side of the neck. The lower jaw was cut through one inch from the median line and one inch above the angle. The mucous membrane was cut through close to the jaw, as it was not involved. The involved portion of the lower jaw with the tumor mass, overlying skin, submaxillary and parotid glands, and numerous lymph glands along the sternomastoid were removed. The wound was entirely sutured externally and within the mouth. The patient collapsed from the extensive loss of blood, but recovered and the wound healed satisfactorily.

Recurrences in the neck were noticed in about two months, and death occurred four months after operation.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

CASE VII.—Male, aged sixty-two years. Was operated upon in East Orange, N. J., in April, 1913, for a movable tumor in the left side of the neck close to the jaw, which had been noticed for six months. The tumor was pronounced a spindle-cell sarcoma. The swelling under the jaw never entirely disappeared, and for four

months it seemed to grow more rapidly. Seven months after this operation it measured three inches by two inches and was attached

Front view, mouth and eyes closed.

Side view, mouth and eyes closed.

Front view, mouth and eyes open.

Side view, mouth and eyes open.

FIG. 5.—Patient No. VII, fourteen months after resection of two inches of the lower jaw for recurrent sarcoma attached to but not involving the bone.

to the jaw and to the skin. Small enlarged glands, freely movable, were felt on the right side in the submaxillary region. The inside of the mouth was normal.

Operation at New York Skin and Cancer Hospital November 6, 1913. Two curved incisions were made from the point of the chin to the angle of the jaw, enclosing a piece of skin measuring three inches by two inches. This skin with the tumor and two inches of the jaw bone were removed in one piece. The jaw was cut through just above the angle and just in front of the first molar tooth. The mucous membrane of the mouth was peeled from the jaw so that the mouth was not cut into, the only opening being where the single tooth remaining on the excised portion of the jaw, protruded through the mucous membrane. A part of the parotid gland and one inch of the internal jugular vein were also removed. The wound was entirely sutured with a small drain in the centre of it. The tumor was found to be a spindle-cell sarcoma.

The wound healed primarily excepting for a sinus in the centre, which persisted for two months. Nodules like enlarged glands gradually developed along the left sternomastoid, and a second operation for their removal was performed at New York Skin and Cancer Hospital, June 9, 1914. Through an incision from the left angle of the lower jaw nearly to the clavicle a chain of glands was removed. Some of these involved a part of the sternomastoid muscle, into which the tumor had spread. A portion of the muscle was removed, and the outer part of the sheath of the vessels for a considerable distance was also removed. As the spinal accessory nerve passed through the tumor a portion of it was removed. The glands on the right side of the neck, not having increased in size since the previous operation, were not dissected. Primary union resulted.

Pathological diagnosis by Dr. Jessup: recurrent sarcoma of the neck.

Nine months after this last operation there is no evidence of recurrence. Motions of the lower jaw from side to side, forward and backward, and upward and downward, are almost perfectly performed (Fig. 5).

Case VIII.—Male, aged fifty years. Following the extraction of a tooth from the left side of the lower jaw there was a persistent soreness of the gum and two months later a rapidly increasing swelling. Four months after the tooth was extracted the swelling was lanced externally. Blood and a little pus escaped and the opening never closed. Five months after the extraction of the tooth there were three openings in the left cheek, discharging pus and blood. The cheek and jaw were much swollen and the top of the gum from the angle of the jaw nearly to the median line was an ulcer with raised, irregular edges.

Operation at New York Skin and Cancer Hospital September 22, 1913. A portion of the left cheek measuring two by three inches, the left half of the lower jaw, excepting the upper part of the ascending ramus, and a mass of submaxillary glands, were removed.

The mucous membrane was entirely sutured and a flap of skin from the neck was swung upward to close the gap in the cheek.

Pathological diagnosis by Dr. Jessup: epithelioma of the jaw and masseter muscle, prickle-cell type.

Three months later the patient returned to the hospital on account of a recurrence just back of the chin and beneath the tongue. One-half inch more of the bone was removed together with a good deal of the floor of the mouth and the deeper tissues. Two weeks after this operation the patient had a sharp attack of dermatitis of the face and neck, probably an erysipelas.

FIG. 6.—Patient No. VIII, sixteen months after resection for two inches of the horizontal ramus and one inch of the ascending ramus for epithelioma of the jaw and cheek. In two subsequent operations the left half of the bony chin and part of the lip, tongue, and floor of the mouth were removed. No apparent recurrence since the last operation, more than a year ago. Motions of the jaw are good, but the size of the mouth is much reduced by removal of one-half of the lower lip and a small part of the upper lip.

Three months after this second operation I again operated for a recurrence in the left side of the chin, extending through the floor of the mouth toward the base of the tongue. This was dissected out very much as one cuts the core from an apple. The tissue removed contained epithelioma.

Thirteen months after the last operation the patient was in good health and apparently free from recurrence, his wounds being entirely healed (Fig. 6).

CASE IX.—Male, aged fifty-four years. Patient noticed a small "pimple" near the right lower wisdom tooth, for which in the succeeding two years he had two local operations and a cauterization. One pathological report was "non-malignant" and the other was

"adamantinoma." The growth recurred in the site of the lower wisdom tooth with slight ulceration and the patient was unable to separate his front teeth more than one half an inch.

Operation at New York Skin and Cancer Hospital October 2, 1913. The tumor with a fair margin of sound tissues including the remains of the tonsil and parts of the pterygoid muscles were removed. The upper part of the jaw bone in the vicinity of the tumor was chiseled away. Dr. Jessup reported the tumor to be of epithelial type, probably malignant. The wound closed rapidly but did not entirely heal and the jaws gradually became more fixed so that they could scarcely be opened at all. A sinus persisted and granulations began to appear in it.

Operation at Miss Alston's Sanitarium April 23, 1914. A vertical incision from a point one inch in front of the ear was extended five inches downward into the neck. Branches of the external carotid artery and numerous veins were ligated. The parotid and submaxillary glands were dissected free and the inferior maxilla was cut through one inch in front of the ascending ramus. Its posterior portion was disarticulated and removed. Examination of the specimen showed that the lower jaw was hollowed out near its angle by a new growth which had deeply infiltrated in the region of the pterygoid muscles. The operation was difficult on account of the fixation of the jaw and the patient lost a good deal of blood. He recovered promptly and sat up in a chair for an hour on the third day. On the fourth day before leaving his bed he had an attack marked by pallor, weak pulse and respiration, without immediate loss of consciousness. Stimulants had no effect and patient died in about two hours, apparently from pulmonary embolism.

CASE X.—Male, aged thirty years. A growth developed in the posterior part of the mucous membrane of the right cheek. At the end of three months it was ulcerating and measured about one and a half inches in diameter. The skin, tongue, and jaw bone were apparently not involved.

Operation at New York Skin and Cancer Hospital July 30, 1914. An incision was made from the angle of the mouth backward across the cheek. Skin flaps were dissected upward and downward and mucous membrane was incised one-fourth inch from the tumor, which was then dissected from the lower jaw and pterygoid muscles. The suture of skin was complete and that of the mucous membrane was carried out as far as possible.

Pathological diagnosis by Dr. Barber: epithelioma, prickle-cell type.

The wounds healed primarily but in three weeks there was an evident recurrence on the jaw bone and September 8, 1914, an incision was made from the angle of the mouth downward and outward to the angle of the jaw and then downward along the sterno-

mastoid. A portion of skin overlying the tumor was excised, together with the submaxillary glands, a portion of the parotid, the jaw bone from back of the canine tooth to the middle of the ascending ramus, and a wide area of mucous membrane, all being removed in one piece.

Pathological diagnosis by Dr. Jessup: carcinoma of the lower jaw, involving the glands.

Wound healed primarily except at the drain site, but there was a rapid recurrence within the mouth in the site of the previous operation. The patient was so troubled with a foul discharge and a great deal of pain that six weeks later a large mass of tumor was cut out through the mouth and through the external wound. Relief was only temporary, and three weeks later a wider excision was practised, including the upper portion of the lower jaw and pterygoid muscles, both of which were badly infiltrated with the tumor. The pain and discharge were markedly relieved by the operation but in two weeks the space gained was again filling with tumor tissue, and the patient died six months after the resection.

Case XI.—Male, aged fifty-four years. A growth in the region of the left tonsil, existing for a year, involved the tonsil, the anterior pillar, a part of the soft palate, and the mucous membrane between the upper and lower jaws and that of the lower jaw as far forward as the second molar, and the adjacent portion of the floor of the mouth and side of the tongue.

Operation at New York Skin and Cancer Hospital July 21, 1914. An incision starting one and a half inches from the chin was extended backward along the lower jaw to the angle and downward along the sternomastoid muscle. Skin flaps were dissected upward and downward. The parotid gland and facial nerve were exposed The dissection was continued across the cheek below these structures so as to save at least the upper branches of the facial. The jaw was cut through in front of the second molar and through the ascending ramus about one inch above the angle. An incision was made completely around the tumor in the mouth, and the whole mass of excised tissue was removed in one piece after division or the anterior branches of the external carotid and its terminal portions. The wound was partially sutured and drained.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type. Hyperplasia of nodes.

The patient had to be fed several days through a rubber tube, passed through his nose nearly to the stomach, as he could not swallow. His recovery was rather slow on account of difficulty in taking nourishment. Seven weeks after operation a piece of bone measuring one inch by one-half inch, dead and entirely loose, was pulled out through the mouth from the cut section of the ascending ramus.

Nine months after operation there was still a small sinus, but no evidence of recurrence (Fig. 7).

Front view, mouth and eyes closed.

Side view, mouth and eyes closed.

Front view, mouth and eyes open.

Side view, mouth and eyes open.

FIG. 7.—Patient No. XI, six months after resection of two inches of the horizontal ramus and one inch of the ascending ramus for epithelioma of jaw, tonsil, and adjacent parts. The whole pouch of mucous membrane between the cheek and tonsil, back of the jaws and which allows them to be separated, was excised. The resulting scar limits motion to an extent not seen after the usual resection; but the range of motion has increased since the photograph was taken.

CASE XII.—Male, aged fifty-five years. The patient noticed a rough spot in the left cheek which gradually increased in prominence and later began to ulcerate. One year after it was first observed the growth measured three-quarters of an inch by one-half inch, being freely movable on the upper portion of the cheek, but glands were enlarged below the jaw.

Operation at New York Skin and Cancer Hospital November 13, 1913. A horizontal incision was made below the jaw and a second one from this upward across the cheek. The tumor with deeper tissues of the cheek down to the jaw bone, and a mass of fat and small hard glands from beneath the jaw were removed. The wound was sutured with drainage, and was slow in healing.

Pathologist reported the growth in the cheek to be a prickle-cell epithelioma, while the glands from the neck showed only hyperplasia.

In May, 1914, the patient went to another doctor, who removed a gland from above his clavicle under a local anesthetic.

In August, 1914, there was a recurrence in the posterior part of the alveolar process of the jaw and a hard area in front of the ear and another one above the left clavicle where the gland was removed.

Second operation at New York Skin and Cancer Hospital, August 13, 1914. Incisions from the angle of the mouth were carried backward curving upward and downward so as to include a part of the cheek and neck. The jaw bone was cut through behind the canine tooth and in the middle of the ascending ramus. Several branches of the carotid were ligated. The mucous membrane of the cheek and floor of the mouth were cut through at a good distance from the tumor and the excised portion of the jaw with the tumor and glands attached to it were removed. The mucous membrane was sutured completely and the skin was sutured except for a distance of about an inch in the centre of the wound, where tension would have been too great.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

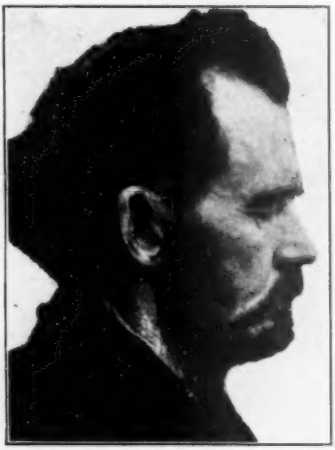
Recurrence rapidly developed and a palliative operation was performed September 10, 1914. Through a transverse incision beneath the chin a small mass of glands with the surrounding fat, fascia, and muscle were excised. The wound healed primarily, but additional points of growth showed themselves in the region of the tonsil, in the floor of the mouth, in the cheek, and also in the neck in front of the mastoid process.

The patient died five months after the resection.

CASE XIII.—Male, aged fifty-three years. The first symptom was a soreness of the inner side of the right cheek. Five months later a carious tooth and a portion of the right lower jaw were removed from within the mouth. Soon after this the cheek and

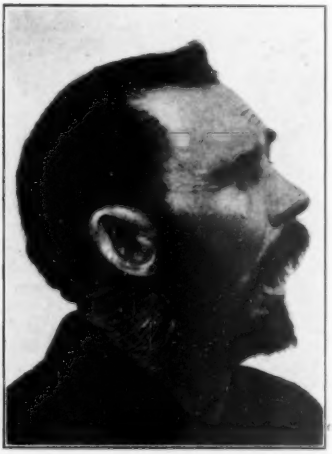
jaw began to swell. Three months after this operation the mucous membrane covering the posterior half of the horizontal ramus, and a little of the ascending ramus of the right lower jaw, was the

Front view, mouth and eyes closed.



Side view, mouth and eyes closed.

Front view, mouth and eyes open.



Side view, mouth and eyes open.

FIG. 8.—Patient No. XIII, five months after removal of the right side of the lower jaw from the second bicuspid tooth to the articulation, for epithelioma of the cheek and jaw bone, involving the pterygoid muscles. Paralysis of the mouth and eye has diminished somewhat, and function is constantly improving, but lateral deviation is still marked.

seat of a leukoplakia, in the centre of which there was a papillomatous and ulcerating area. There were enlarged lymph glands in the region of the parotid, and about the bifurcation of the carotid. There was a small leukoplakia on the left lower jaw but no ulceration nor papilloma.

Operation at New York Skin and Cancer Hospital August 15, 1914. The skin was dissected back by an incision starting from the lobe of the ear, following the posterior and lower edges of the lower jaw to about the middle of the horizontal ramus and then curving downward to the centre of the sternomastoid. The neck was freely dissected from the hyoid bone to the ear. The branches of the external carotid and the internal jugular were divided. The parotid gland was removed from behind forward, the muscles of the jaw being cut just below the malar bone and dissected downward before the mouth was opened. The mucous membrane was then cut through wide of the involved area, the jaw sawed behind the second bicupsid, disarticulated, and removed with the attached portions of tumor and other soft tissues. Hemorrhage was profuse, and in spite of clamps and ligation the patient lost considerable blood, and the upper portion of the wound had finally to be packed with gauze. The mucous membrane of the mouth was easily sutured and the skin was sutured excepting for the drain site.

The patient made a good recovery, rapidly overcoming his operative anemia. The wounds where sutured healed primarily with very little leakage from the mouth.

Examination of the specimen showed the bone to be badly penetrated and there was excessive involvement of the pterygoid muscles.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type. The enlarged lymph glands were hyperplastic only.

Eight months after resection the patient was in good condition. There was no sign of recurrence externally or internally. A minute sinus persisted at the upper end of the external scar in front of the ear, and there was a narrow streak of leukoplakia about one-third of an inch long in the mucous membrane just behind the point where the jaw was sawed through (Fig. 8).

Case XIV.—Male, aged forty-three years. A dentist called the patient's attention to a growth on the left lower jaw about the site of the bicuspid teeth. Three weeks afterward it was a tumor with a mushroom shape, measuring about three-quarters of an inch in diameter.

Operation at New York Skin and Cancer Hospital October 12, 1914. The growth was removed together with a narrow margin of healthy mucous membrane. The corresponding portion of the alveolar process was chiseled away.

Pathological diagnosis by Dr. Jessup: epulis, giant-cell sarcoma.

Six months later the patient was examined and there was no swelling of the jaw nor any other sign of recurrence.

SUMMARY OF CASES OF RESECTION OF LOWER JAW.

No.	Sex.	Age.	Physical examination.	Pathological diagnosis	Extent of resection.	Result.
I	M.	75	Jaw, ulcerating; recurrent after operation.	Epithelioma; bone involved.	2½ in. horizontal ramus.	Death in two months after operation elsewhere.
II	F.	45	Jaw, ulcerating; recurrent after operation.	Epulis; giant-cell sarcoma; bone not involved.	Alveolar process only.	Well; no recurrence for thirty-three months.
III	M.	44	Jaw, ulcerating; recurrent after operation.	Epithelioma; bone involved.	2¾ in. from chin backward.	Death in ten and a half months.
IV	M.	54	Mucous membrane of cheek.	Epithelioma; bone not involved.	From bicuspid teeth to joint.	Well; no recurrence for thirty-two months.
V	M.	34	Cheek; recurrent in jaw after three operations.	Epithelioma; bone involved.	From symphysis to above angle.	Death in nine months.
VI	M.	52	Jaw and glands; recurrent after operation in neck.	Epithelioma; bone involved.	From canine tooth to above angle.	Death in four months.
VII	M.	62	Neck below jaw; recurrent after operation.	Spindle-cell sarcoma; bone not involved.	From bicuspid teeth to above angle.	Operation after seven months for recurrence in neck; well; no recurrence for nine months since last operation.
VIII	M.	50	Jaw, ulcerating in mouth and through cheek; recurrent after operation.	Epithelioma; bone involved.	From near symphysis to above angle.	Two other operations for local recurrence in six months; well; no recurrence for thirteen months since last operation.
IX	M.	54	Jaw, ulcerating in mouth; recurrent after operation.	Carcinoma; bone involved.	From bicuspid teeth to joint.	Death in four days from embolism.
X	M.	30	Cheek, ulcerating in mouth; recurrent after operation.	Epithelioma; bone not involved.	From canine tooth to above angle.	Extensive local recurrence in spite of two more operations; death in six months after resection.
XI	M.	54	Cheek; gums; tonsil; tongue; soft palate.	Epithelioma.	From second molar to above angle.	Well; no recurrence for nine months.
XII	M.	55	Cheek and jaw, ulcerating; recurrent after two operations.	Epithelioma	Canine tooth to above angle.	Extensive local recurrence in spite of two more operations; death in five months after resection.
XIII	M.	53	Cheek and jaw, ulcerating in mouth; recurrent after operation.	Epithelioma; bone involved.	From bicuspid teeth to joint.	Well; no recurrence for eight months.
XIV	M.	43	Jaw in mouth.	Epulis; giant-cell sarcoma.	Alveolar process only.	Well; no recurrence for six months.

CERTAIN MEDICAL ASPECTS OF RECURRENT MALIGNANT TUMORS.

By James B. Herrick, M.D.,
CHICAGO.

It is frequently the experience of physicians to see a patient from whom a malignant growth has been removed long before, in whom recurrence has taken place, not at the site of operation, not in the shape of visible and palpable tumor masses in distant parts of the body, but with symptoms that resemble those of a so-called medical or internal disease as distinguished from the external or surgical, *i. e.*, operable affection. To such manifestation the term medical or non-surgical recurrence may be applied, though such a use of the term recurrence is open to criticism, because in the strict sense it is not a recurrence. The distant foci of tumor cells were already established at the time of operation, though dormant, but are now aroused into activity; or tumor cells slipped into the circulation during the manipulation of the operation and, lodging in distant parts, later as metastases, produce the symptoms to which reference has been made. So, also, these are really borderland cases and not strictly medical.

It is the purpose of this paper to call attention in a brief and practical manner to some of the very varied clinical manifestations of such recurrences as they might be met with in general practice. It is hoped that it may contain some helpful hints as to diagnosis.

Four things are likely to stand in the way of the early and easy recognition of the presence of these so-called medical recurrences: (1) The fact that there is no recidivation at the site of operation; (2) that no tumor mass can be made out in other parts of the body; (3) the long duration of time that may have elapsed since the operation, during which time the patient has apparently been healthy, and (4) the fact that the symptoms are not those commonly associated with tumor, but rather those of some other, often a so-called medical, condition.

The first three stumbling-blocks to diagnosis should be easily avoided by remembering that they are by no means exceptional, and should not be given much weight in excluding the presence of neoplasm. The thoroughness with which surgeons today remove tumors, *e. g.*, of the breast, makes recurrence *in situ* comparatively rare when an early diagnosis has made an early operation possible. A soft, pliable scar with no regional glandular involvement proves the concientious carefulness with which the surgeon has done his work, but does not exclude metastases elsewhere. And these metastases need not be large masses in order to produce symptoms. We are familiar with the large tumor in the abdomen that comes

after the removal of a sarcomatous testicle; or the indurated mass found in the pelvis on rectal or vaginal examination, which represents the recurrence after the operation for carcinoma of the uterus or rectum; or the enlarged liver that appears after the removal of a melanotic sarcoma of the eye or a cancerous pylorus. But failure to find such frankly neoplastic deposits should not cause us to rule out the presence of smaller and hidden ones. Nor should a lapse of many months or even two or three years throw us off our guard and cause us to feel secure against return of malignant growth. Longer periods than this may elapse before there is evidence of metastatic activity. I have known eight years to pass after the removal of a carcinomatous breast before the patient succumbed to metastases which were evident only at autopsy.

The fourth difficulty is one not so easily surmounted. At times it is only by careful exclusion of other diseases, or by patiently tracing some atypical symptom or sign to its malignant source, that a correct diagnosis is made. And often this diagnosis can be only a presumptive one.

Some of these clinical features are worthy of special consideration. Among them are nervous symptoms, which may often accurately resemble those of other diseases. Thus pain in the lumbar, sacral, and gluteal region may readily pass for sciatica. It may, in fact, be genuinely sciatic in origin, a nodule pressing on this nerve or tumor cells invading the nerve sheath. At times, however, a careful examination will show a tenderness that is in the sacrum or the lumbar vertebræ, rather than in the nerve itself. It represents a bone metastasis, with perhaps pressure on the nerve roots as they leave the vertebral canal. One of the confusing features in some of these cases of severe lumbar and sciatic pains (and the same is true of Pott's disease and the spondylitis of typhoid) is the fact that the patients often become "nervous," sleepless, complaining, even hysterical, craving morphin, and the thought of the whole trouble being functional, a sort of railway-spine affair may be entertained. The true nature of the lesion may be revealed only when a pressure paraplegia supervenes. Neuralgic pains in other parts of the body, as in the intercostal nerves or in the scalp, may have their origin in deposits of tumor in bone. That certain tumors, as of the breast, thyroid, prostate, and adrenal, are prone to form metastatic deposits in bone is well known. No pain, therefore, occurring in a patient who has been operated upon for a malignant growth, and especially a growth in one of these organs, should be passed as due to simple neuralgia until careful search has been made to exclude bone metastases. At times an irregularity or swelling of the surface of the bone over the spot of tenderness will be helpful. The bone may crackle or fracture under even light pressure, as I have seen happen in the case of a rib. The roentgenogram may show focal changes in the bone and

myelocytes or other blood change may be suggestive of involvement of the marrow in disease. A somewhat confusing feature is the disappearance of pain over the site of a bone deposit and the variation in tenderness that may materially change from day to day. Perhaps variation in circulatory conditions may explain these changes; and one may conceive of the tumor mass breaking through a surrounding shell of bone, the pain lessening as the pressure is relieved. Cerebral symptoms may be variable, *e. g.*, symptoms of brain tumor from metastatic deposits. In one case, months after an amputation of the breast, in which local recurrence had taken place, a sudden plugging of the central artery of the retina occurred, presumably by tumor cells.

Another group of symptoms, often confusing, concerns the respiratory tract. Long after the operation a patient may be taken with a cough, and then develop what seems to be an ordinary bronchial catarrh. The cough persists, dyspnea appears, and there is some cyanosis. The sputum is scanty, or it may be mucus or blood-tinged. Rales, dry and moist, may be heard in various parts of the chest, and possibly here and there is made out an area of harsher respiration, or perhaps a spot of dulness. There is little or no fever as a rule. Dyspnea may increase and the respiration grow hurried. There is some loss in weight. It is necessary for one to see an autopsy on only one of these cases, with the lung riddled with small or larger tumor nodules, to be able to understand how the condition resembles clinically miliary tuberculosis. Of course, larger masses may produce symptoms that are more clearly those of tumor. These larger tumors are more easily recognized, or at least suspected, from the predominance of pressure symptoms. The Roentgen rays in both types of thoracic metastases may be of material help in diagnosis.

Another metastatic phenomenon, often a late one, and often the first sign of failing health after the operation, is pleural effusion. Local pain with friction rub may clearly indicate involvement of the pleura; or dyspnea and dry cough may lead to an examination of the chest and a pleural cavity may be found to contain a large amount of fluid, no pain worthy of the patient's notice having been complained of. At times pain, some fever, or rapidly developing dyspnea will make the process resemble tuberculous pleurisy; or even a pneumonia may be thought of if bronchial breathing be detected in some part of the affected side. Rheumatic, tuberculous, and traumatic origin for the pleural fluid, as well as the ordinary causes for hydrothorax, must be excluded as accurately as possible. Bloody fluid obtained by exploratory puncture, the fluid perhaps containing tumor cells or large multinucleated cells, with mitotic figures, and lacking the lymphocytes and tubercle bacilli of tuberculous fluid, may be of material help. Often the fluid recurs even after repeated tappings that may be necessary

for the relief of pressure. At times it will disappear. Such a disappearance took place in a remarkable case which I saw of late metastases months after the removal of a malignant syncytioma. Sudden large pleural effusion with pain and some fever followed the carriage into the pleura of the tumor cells. These apparently gravitated to the bottom of the pleura, where a large growth developed, invading the diaphragm and the lumbar vertebra, leading ultimately to paraplegia and death. No tumor mass was ever made out on physical examination during life, and no pelvic recurrence took place. The autopsy revealed the above chain of events.

Pleural fluid, therefore, in one who even years before has had a malignant tumor removed should arouse the suspicion of pleural metastases, nor should the temporary disappearance of this fluid lead to a too confident quieting of this suspicion.

Another remarkable phenomenon was seen in a young man of about twenty years, who consulted his physician for slight temperature, cough, and symptoms suggestive of incipient tuberculosis. A sudden and severe hemoptysis occurred. The acute anemia was extreme and out of all proportion to the amount of blood lost externally. Dyspnea was pronounced. The explanation was found in a hemopneumothorax. The lung had ruptured and a large amount of blood with air was in the pleural sac. Death from anemia seemed imminent, but after many days of delirium, prostration, and fever, due to the absorption of the blood, improvement occurred and the boy returned to his home. The explanation for this odd occurrence was found in a metastatic sarcoma of the lung. Five years before the boy's thigh was amputated for sarcoma of the tibia. No local recurrence. A few months after the pulmonary accident just described the boy died with every evidence of thoracic tumor. I have seen another case of metastasis in the pleura with fluid long after amputation of the leg for sarcoma, and one after removal of the testicle.

Just as a pleurisy, especially an afebrile pleurisy, should in these patients arouse a suspicion of the localization of secondary tumors in that tissue, so an otherwise unexplained ascites should lead to a careful examination for proof of the malignant origin of the abdominal fluid from direct involvement of the peritoneum or pressure on the larger trunks of the portal vein. Bloody or chylous fluid may be significant.

Personally, I have never seen clinical symptoms from involvement of the heart by tumor metastases following operation, though at autopsy symptomless nodules in the myocardium or pericardium are occasionally met with. Nor have I noticed clinically symptoms that could be referred to metastases in the kidney.

One type of disease due to these metastases is characterized chiefly by severe anemia and marasmus. This I have seen in a recurrence after removal of carcinoma of the breast. In this in-

stance symptoms like diabetes insipidus were present for many weeks. While autopsy of the body showed numerous nodules, the brain was not examined. Perhaps here was the tumor that induced the polyuria, by pressure on the hypophysis. In another case a profound anemia much resembling pernicious anemia came on months after an operation for carcinoma of the penis.

Occasionally there is reluctance to accept a diagnosis of post-operative metastasis, because a nodule appearing after the operation in some distant part of the body has for a long time remained stationary in size, or has even at times seemed smaller. This should not, of course, rule out a malignant growth. The glands in the neck that are secondarily carcinomatous, as with primary cancer of the stomach, do not, of necessity, grow rapidly. I have seen a carcinomatous gland in the left side of the neck remain the size of a hickory-nut for a year, its first appearance being a few months after the removal of a breast for carcinoma. This patient had also carcinoma of the vertebra, with later paraplegia.

Every physician knows the danger there is in asking a patient what in the law courts are called leading questions. Unconsciously we may suggest answers to such a patient, or lead the history away from facts that would otherwise be clearly brought out by the patient's unguided recital of the history. But there are times when direct questioning is necessary and where it must be pressed. We know how a patient who fears tuberculosis will dodge and evade a direct answer that seems to him incriminating. One must often push the questions and insist upon definite answers.

Similarly, unless direct questioning is resorted to, one may sometimes fail to learn of the previous operation; the patient may forget to speak about it, or regard it as insignificant, or may be purposely concealing the fact. Even the physician may at times be inclined to underestimate the importance, from a diagnostic point of view, of the removal of a seemingly insignificant pigmented mole, or a "polypus" from the neck of the uterus. And the patient may have been given to understand that the tumor was innocent, though a telephone conversation with the surgeon who operated, or a reference to hospital records, might reveal the malignant character of the growth. A fear of learning the serious nature of the illness may induce a patient purposely to make false or misleading statements regarding previous operations, or to conceal the scars of these from the eye of the examining physician. I well remember a case of left-sided pleural effusion in a woman whose left breast had been removed some time before for carcinoma. The careful doctor had made several examinations of the chest, but through seeming modesty, as became a maiden lady of fifty, the clothing was on the occasion of these examinations always deftly arranged by the patient so that the scar of the operation was covered. Great was the surprise and embarrassment of the doctor as this scar

came into view when, at the consultation, in response to insistent requests, the clothing was removed from the chest. The clue to the nature of the pleural effusion was evident. The possibility that a scar may mean the previous removal of a malignant growth should always be taken into consideration, whether such scar be on the lip, the scrotum, cervix uteri, the breast—in fact, anywhere. An absent eyeball has more than once led to the diagnosis of melanotic sarcoma of the liver.

In conclusion it may not be amiss, after having referred so often to the necessity of a thorough examination of these patients in whom there are obscure postoperative manifestations of malignant tumors, to call attention to the importance of such investigation before operation. A thorough exploration of the pelvis per vaginam and per rectum would sometimes ward off the useless operation for carcinoma of the stomach or breast. Secondary peritoneal tumors, as is well known, may sometimes plainly be made out on rectal examination. Such examination may readily be omitted when there are no pelvic symptoms, and when a palpable tumor of the stomach invites to operation. Unless obstructive or other urgent indications point to removal of the primary growth the detection of secondary deposits will contraindicate the operation. In three cases of hypernephroma I have seen operative removal of the kidney vetoed, once because of a secondary tumor in the brain, another time because of secondary deposits in the lung, and in a third case, the deciding voice being that of the late Christian Fenger, because edema of the leg made growth into the vena cava probable, and autopsy showed this to be the case. In a recent case secondary tumors in the lung decided against removal of a carcinomatous tongue. Percussion, auscultation, and the Roentgen rays all clearly showed the invasion of the chest. Such a warning as this may seem uncalled for. But clinical experience has made me feel that it may not be out of place to speak of these things, for it is often the well-known and commonplace that is forgotten, and that from time to time needs to be brought back to our attention.

VALUE OF RADIUM, SUPPLEMENTED BY CROSS-FIRE ROENTGEN RAYS, IN TREATMENT OF MALIGNANCY.[1]

By Russell H. Boggs, M.D.,

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Much discussion has taken place in regard to the comparative value of radium, mesothorium, and the Roentgen rays in the

[1] Read before the Allegheny County Medical Society, January 19, 1915.

treatment of malignancy, but in view of the present knowledge of radio-active substances and the Roentgen rays, it is impossible to advocate the extended use of one to the exclusion of the other. Each agent has its place. Both forms of radiation have wide ranges of usefulness which differ under certain conditions and in adaptability to parts affected. When the gamma rays of radium are filtered from the alpha and beta it is found that they conformed in most respects to that of the Roentgen rays. During the past few years physicists have proved that both the Roentgen rays and the gamma rays are ether impulses identical in nature, differing only in wave length and power of penetration.

While today we are using Roentgen rays of much greater penetrating power and filtering out the lower inefficient rays, we must use different apparatus before we can produce rays with as great penetrating power as the highest gamma rays of radio-active substances. Many claim that the highest rays are unnecessary and have no therapeutic effect. This is a question still unsettled. Dessauer, of Frankfort, Germany, has constructed an apparatus which he claims produces rays which are, by every physical and biological test, identical with the gamma rays. He was to demonstrate this at the last meeting of the American Roentgen Ray Society in Cleveland, but, on account of the European War, was unable to be present.

The new tube invented by Coolidge, and used in many laboratories during the past year, marks a great advance because it provides much more uniform radiation which is essential in deep therapy. Coolidge is experimenting with a ray of much greater penetrating power than anything known except that produced by Dessauer, but has not placed this tube on the market. In a letter which I received from him recently he stated he would soon have this tube perfected by which any degree of penetration can be obtained.

With our present apparatus the therapeutic effects with the highest filtered Roentgen rays closely approach those of radium. There is no question that heavy doses of the filtered rays extending over not too long a period will cause the healing or disappearances of many malignant conditions which were unaffected by the inefficient treatment given a few years ago. After selecting the case, success or failure is rather a matter of technique, whether using radium or the Roentgen rays.

Both radium and the Roentgen rays as they are now understood have a different place in medicine and surgery than they had a few years ago. Those using radium had only small quantities, and often it was not of good quality, and the operators knew little or nothing about the necessity of filtering out the soft rays which did not penetrate, but which really predominated and acted as a caustic on the superficial tissues, nor did they understand much

about secondary radiation. The same was true with those using the Roentgen rays. Any kind of a vacuum tube was used, no filters were employed, and usually the rays were directed in one direction toward the growth instead of using the present cross-firing methods, and with the tube placed at any distance regardless of the intensity without any instruments being used to measure the dosage.

There has been some rivalry between those using radium and the Roentgen rays, and as fast as one progressed the efforts of the other party to overtake its rival became more active. The inefficient Roentgen-ray work done in the early days and that which is being done at the present time by many accounts for some of the radium advocates making statements that there is no comparison in results between those produced by radium and the Roentgen rays. Many radium enthusiasts who are just beginning are making extravagant claims for radioactive substances because they have seen a few brilliant results for the first time, and they might be compared to the early Roentgen-ray extremists. Radium is an extremely valuable agent in the radiotherapeutic field, and extravagant and unwarranted claims will do much to hinder the avdancement of this branch of medicine. It can readily be seen that many physicians are judging both agents wrongly by the work being done by unqualified operators.

The experienced radiotherapeutists are the ones to whom we must still look for true information, rather than in books and the many periodicals lately published. The field of radiotherapy, meaning treatment by both radium and the Roentgen rays, is at present a kind of no one's ground and is suffering from incursions from every province of medicine and owning definite allegiance to none.

In treating a case either by radium, mesothorium, or the Roentgen rays we must always face a series of problems. Given a case with a certain lesion, its position, extent, its susceptibility to the influence to this or that radiation, when we must determine the agent or agents to use. The duration and method of application can be varied almost to infinity. This enables us to realize how rich radiotherapy should be in its results when properly selected and employed. In this connection let me quote several paragraphs from Dr. Francis Hernaman-Johnson in the October number of the *Archives of the Roentgen Ray:*

"It is, at any rate, certain that in cancer the therapeutic effects of hard filtered Roentgen rays closely approach those of radium. On the other hand, a wide gap yawns between the Roentgen-ray results of today and even those of a few years ago. A claim often set forth in papers and books on radium therapy is that rodent ulcers have been cured by radium after months of Roentgen-ray treatment had proved ineffective. My own experience would

lead me to believe that sharp doses of filtered Roentgen rays extended over a period not exceeding one month will cause the healing of any rodent ulcer which is amenable to radioactive substance in any form. . . . The employment of rays which are too soft, or those of insufficient doses extending over a long period, does positive harm. If, however, the mischief is not too far advanced a few large applications of filtered Roentgen rays may cause healing, just as effectively as gamma rays."

In speaking of postoperative treatment Dr. Hernaman-Johnson describes the form of radiation in the following words: "An approximately uniform dosage throughout the whole of the suspected area is, therefore, the ideal to be aimed at. For the complete realization of this ideal two things are necessary: (1) rays so penetrating that they will pass right through the body with the loss of only a small fraction of their value, and (2) a parallel beam of such rays so that they shall not lose energy by spreading. Gamma rays fulfil the first condition. They will pass through 60 cm. of tissue before losing half their original intensity; but, to satisfy the second requirement, it would be necessary to suspend the tube some twenty inches from the skin, a procedure which would render useless even so large a quantity as 1000 mg. of radium salt. Hard Roentgen rays, on the other hand, though they fall to half value when they have penetrated about 10 cm. into the body, can be produced in any desired amount, so that what is to all intents and purposes a parallel beam may be played upon selected areas. Existing Roentgen therapy thus approaches much more nearly the requirements of prophylaxis than treatment by radium."

Then Dr. Hernaman-Johnson continues: "One of the great advantages claimed for radium over Roentgen therapy is that a tube of the radioactive substance may be buried within a cancerous tumor. In accordance with the law of inverse squares, the activity of such a tube diminishes rapidly toward the outer parts of the growth; so that the risk, on the one hand, of not killing outlying cancer cells, and, on the other, of seriously injuring healthy tissues, is one to be very carefully considered.

A study of the literature of radium therapy in cancer shows that both these happenings are not remote contingencies, but have actually, in numerous cases, been the cause of failure. If all tumors were perfect spheres it might be possible to calculate the exact quantity of radium required; but, unfortunately, cancer masses fail to conform to any of the figures with which we are familiar in text-books of plane and solid geometry. The recently introduced treatment by radioactive needles is open to the same objections, though in less degree. The only safe method, as in uterine cancer is to avoid huge doses, and to supplement the action of the radium tube by Roentgen-ray cross-fire outside."

Many observers who have used both agents extensively agree

with Dr. Hernaman-Johnson, whose conclusions quoted are so clearly stated.

Every radiotherapeutist knows that the beam of rays given off from a Roentgen bulb or a radium tube is a mixture of heterogeneous rays, and that it is only by filtering and increasing the distance between the source of radiation that we can approach anything like a homogeneous ray. Then if we have homogeneous radiation we must not neglect the diminution of the distal dose by absorption by the tissues. There is always a difference between the proximal and distal dose. In using proper filtered radiation it has been estimated that each centimeter of tissue absorbs from 5 to 10 per cent. of radiation; so it can be readily seen that the deeper the growth is situated the more cross-firing with any form of radiation is necessary.

Dessauer considers that it would be necessary to have a radium tube containing 5 grams of radium when properly filtered and placed at the proper distance to give off a homogeneous ray equal to a bulb placed at the proper distance and properly filtered. No one has this amount or is it obtainable. This explains why most of the European workers who have had the best results in the treatment of malignancy long ago realized the importance of using the Roentgen rays from outside as an adjunct, and administering it through as many ports of entry as possible. In many places in the treatment of uterine cancer they used over forty ports of entry. This is a radical change from the technique that was used when the first cases of uterine cancer were treated by Roentgenotherapy years ago when little more than superficial or skin effect were produced. The treatment was given with an unshielded tube placed anteriorly to the abdomen the same as when making a radiogram.

It is generally accepted that equally good results can be secured by the use of radium or the Roentgen rays in the treatment of external epitheliomas, but, as a rule, most epitheliomas are treated by the Roentgen rays. It means nothing when some enthusiastic advocate of either the Roentgen rays or radium states that there is no doubt that one agent has been effective, whereas the other completely failed. Most likely the one applying the agent failed to recognize the limitations of his therapeutic agent, but when the epithelioma is situated on mucous membranes in cavities, radioactive substances will usually effect a cure unless too far advanced. Here radium always should have the preference. I believe no time should be lost in treating every case by radium as soon as diagnosed. The Roentgen rays should not be used through a speculum, thus losing valuable time if radium is available. I see so many patients coming late where the physician or surgeon had made an early diagnosis, and not knowing the value of radium, giving treatment by some other means when the lesion was situated so that it was inaccessible to any other form of treatment. Leukoplakia is a condition which can be cured by a few applications of radium or

mesothorium and responds so unsatisfactory to any other therapeutic method. If left untreated the liability to ultimate malignant change must always be remembered. The stage at which an epithelioma situated on a mucous membrane is diagnosed and treated determines the prognosis more than any other malignant condition.

In carcinoma of the mouth, throat, rectum, or vagina the radioactive substance can be placed within the lumen of the organ or in close proximity to the growth, and, I believe, is superior to the Roentgen rays as far as the local treatment is concerned. But in all these cases—particularly if the disease is advanced and the lymphatics involved—the Roentgen rays are superior to any quantity of radium anyone has used up to the present time for the treatment of lymphatic glands. It must also be remembered that these high penetrating rays, given in great quantities and properly filtered, not only effect the adjacent lymphatic glands but also have a marked effect on the local tumor. In other words, it seems that the treatment is not complete if the radium is used locally unless it is followed for a certain length of time by Roentgenotherapy. Radium might be compared to surgery in its action on the local tumor. The great advantage of the combined treatment is thus self-evident. Some inoperable cases of carcinoma which have not been cured have been improved to such a degree that a subsequent operation could be performed. No matter how rare these cases may be, every case should at least have this amount of palliation. It is certainly true that the diagnosis of an inoperable malignant growth should not be equivalent to a death warrant to the patient. Postoperative treatment carried out in this manner would undoubtedly increase the number of permanent cures. If radiotherapy could change the percentage of cures in only a small percentage of the cases it is more than justified. It would seem that this is not advising too much when some noted German gynecologists advise radiation as the only method of treatment of operable cases of cancer.

Besides using radium in cavities I have been applying after operation a tube of radium in the axilla whenever it is possible, because it is often difficult or almost impossible in some cases for the patient to raise the arm sufficiently to give the desired amount of Roentgen treatment. Otherwise the results with modern Roentgen treatment are so good that, as far as external treatment is concerned, it seems radium has no advantage. When Roentgen rays are given prophylactically early, local recurrences are rarely seen. The great drawback is that the patients come to operation too late when deep metastasis has taken place. It is not enough in many cases to ray the axilla, the root of the neck, chest wall, and mediastinum, but the stomach and ovaries should receive attention. In order to have the best results the patients should not only come early but the lymphatics must receive radiation as uniformly as possible.

In an article on "Carcinosis of the Bone, Secondary to a Growth in some Epithelial Organ."[2] I mentioned the frequency of bone metastasis, and that it took place late, from three to five years after the cases were seen, and usually in the scirrhous type of carcinoma.

Limacher, who studied metastasis in mammary carcinoma, found the bones involved in about 14 per cent. of the cases. This shows the necessity of raying the cases thoroughly and early after operation, by the most efficient method possible.

In conclusion, the success of radium therapy in the treatment of malignancy is attained chiefly in those cases in which the radioactive substance is brought into contact with the growth, either in or on it, without an intervening layer of healthy tissue, and in which the thickness of the tumor does not exceed 4 cm. It is preferable to use the hard Roentgen rays for all deep-seated growths in which there is an intervening layer of healthy tissue. Radium gives the best results when it is brought in contact with the growth and supplemented by the Roentgen rays from outside by the cross-fire method. It is necessary for the operator to know the relative value of radium and the Roentgen rays when combining these two agents.

BLOOD TRANSFUSION: INDICATIONS; RESULTS; GENERAL MANAGEMENT.[1]

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Blood transfusion, until recently, was expected to be a cure-all, and was tried in almost every kind of desperate condition. As the result of a large amount of work done since Crile's introduction of a successful technic for direct blood transfusion,[2] the real indications for transfusion have become better understood and more sharply defined. Crile's statement of the indications have, for the most part, remained valid, but subsequent

[2] New York Med. Jour., December 2, 1911.

[1] Various parts of this paper were presented at a stated meeting of the New York Academy of Medicine, December 17, 1914, and at the meeting of the Association of American Physicians, May 11, 1915.

[2] Canada Lancet, 1906-07, xl, 1057; Ann. Surg., 1907, xlvi, 329.

experience has altered our views in regard to many of them. In particular the indications for transfusion have been extended by two facts: transfusion has become safe, and transfusion has become a much less serious procedure for both patient and donor. Clinical experience has shown that the tests for agglutination and hemolysis between blood of donor and of patient are reliable,[3] and except in the relatively uncommon emergency case in which there is not time to do these tests, we now approach a transfusion with absolutely no fear of this lurking danger. The danger of excessive transfusion (of which two instances occurred among the earlier of our cases) can be easily avoided—for direct transfusion by a simple method of calculation introduced by us,[4] and for indirect transfusion by accurate measurement of an amount of blood predetermined by such a calculation. The simplifications of technic, and especially the introduction of a good method of syringe transfusion by Lindeman,[5] have made transfusion a procedure which involves little trauma or pain, and which can be repeated on the same patient as often as desired. As a result of all this the tendency is more and more to use transfusion not as a means of last resort but as an ordinary therapeutic measure.

In the present paper we have made a clinical study of 212 blood transfusions in 189 cases which we have had the opportunity of observing either in the hospital or in private practice. These transfusions were done by a number of different surgeons, and for a great variety of different conditions.[6] In many of the cases the indications had been established by previous work: on the other hand some of the transfusions were practically experimental. Of these, some were successful and others, in the light of the experience thus gained were cases in which even under the best possible conditions little or nothing can be expected from transfusion.

We shall refer only incidentally to the now rapidly growing literature, as we believe that more will be gained by presenting our own conclusions fully and leaving it to the reader to compare them with those of others.

We shall first briefly summarize the general results of all the transfusions (Part I) and shall then discuss in detail the results in each of the conditions for which transfusion was done (Part II); and finally (Part III) we shall discuss certain details concerning the general management of transfusions.

[3] Ottenberg and Kaliski, Jour. Amer. Med. Assoc., 1913, lxi, 2138.

[4] Libman and Ottenberg, Jour. Amer. Med. Assoc., 1914, lxx, 764.

[5] Amer. Jour. Dis. Child., 1913, vi, 28; New York Med. Rec., 1912, lxxxi, 979.

[6] We wish to thank the members of the Attending Staff of the Hospital for their generosity in permitting us to utilize the records of the cases that we studied in their services. We are also under obligations to many physicians whose private cases we followed with them.

Part I.

GENERAL SUMMARY OF RESULTS.

One occasionally hears the opinion put forward that transfusion after all has not turned out to be a useful procedure, that there are few cases in which it really does good, and that it will probably be dropped again just as it was thirty years ago after the wave of enthusiasm for it following the Franco-Prussian War. For this reason we present the following general summary of the successes and failures in the 189 cases which we have seen. The proportion of successful results in the future will undoubtedly be far greater than in the past, not only because of recent technical improvements but because the indications will be more definitely known and the discrediting transfusions in hopeless cases, in which transfusions can not possibly be of avail, will not occur. The cases are subdivided according to the following scheme:

I. Successful cases.
   1. Cases in which the prognosis was extremely bad, and transfusion saved life.
      (*a*) Cases which subsequently completely recovered.
      (*b*) Cases in which the original underlying disease continued.
   2. Cases which recovered but in which the prognosis before transfusion was not desperate.

II. Unsuccessful cases.
   1. Cases in which there was temporary improvement following transfusion, with death later from continuation of the original disease.
   2. Cases which died of some disease necessarily fatal and in which transfusion could not have been expected to do much good.
   3. Cases in which transfusion did little or no good, although from the nature of the disease a good result might have been possible.

I. Successful Cases. 1. *Cases in Which Transfusion Saved Life.* There are 42 cases of this kind—that is to say, cases which almost undoubtedly would have died in a short time if transfusion had not been done. Of these, 29 subsequently recovered entirely and were discharged well or have continued under observation up to the present time; 13 were saved from immediate death but have continued to suffer from some chronic condition which could not have been cured by transfusion (pernicious anemia, leukemia, etc.).

(*a*) *Cases Which Ultimately Recovered.* Almost all the 29 cases which were rescued from immediate death were cases of hemorrhage. There were 9 cases of gastric or duodenal ulcer with extreme

hemorrhage; 3 cases of hereditary hemophilia; 3 cases of ectopic pregnancy; 7 cases of hemorrhagic diathesis; 1 case of sloughing uterine fibroid with hemorrhage; 1 case of cholemic hemorrhage; 1 case of hemorrhage after a kidney operation; 1 case of illuminating gas and morphine poisoning; 1 case of typhoid hemorrhage.

(*b*) *Cases in Which Life was Saved by Transfusion, but in Which the Underlying Disease Continued, or Which Ultimately Left the Hospital in Greatly Improved Condition or Are Still under Observation.* These 13 cases include 6 patients with pernicious anemia who lived for long periods after apparently life-saving transfusions; 2 cases of cancer in which persistent hemorrhages stopped; 1 case of hemorrhagic diathesis with grave anemia, who left the hospital in improved condition against advice; 1 patient with a tumor of the spleen and grave anemia of unknown origin and 1 case of chronic leukemia.

The cases, then, in which transfusion was apparently life-saving fall under four main headings:

Acute anemia from hemorrhage.
Hemorrhagic diathesis, whether hereditary or acquired.
Grave chronic anemias.
Poisoning.

2. *Cases Cured or Greatly Benefited, Not in Desperate Condition at Time of Transfusion.* There were 43 cases in which transfusion was not an emergency measure but was performed on patients whose general condition had been seriously impaired by chronic disease. Most of these patients ultimately made complete recoveries, others continued to suffer from the chronic illness. In all the cases there was great improvement following the transfusion.

There were among these, 3 cases of gastric or duodenal ulcer which had repeated hemorrhages but were not in desperate condition at the time of transfusion. Undoubtedly recovery in these cases was greatly hastened by transfusion. The same may be said of 2 cases of dysentery with marked anemia. In this group also were 9 cases of pernicious anemia with marked remissions; 3 of the cases were instances of severe infection from osteomyelitis, in which the increased strength given by transfusion undoubtedly brought about the ultimate recovery; 9 were cases of malignant disease which were greatly benefited by the transfusion, 3 of them undergoing subsequent radical operations.

Of the 189 transfusion cases, then, 85 (or 45 per cent.) were successful in that the condition of the patient was greatly improved, and 42 of these (or 22 per cent. of the whole number) were life-saving.

II. Unsuccessful Cases. There were altogether 104 cases in which transfusion did no good or in which the continuation of the original disease caused death. (This is exclusive of a few early cases, not enumerated in the present series, in which the operation

of transfusion itself was not successful, *i. e.*, no blood, or very little passed from donor to patient.)

1. There is a first group of 28 cases which improved for a short time but died subsequently from continuation of the original disease. These included a considerable variety of diseases, chief among which were malignant tumors, pernicious anemia, subacute streptococcus endocarditis, dysentery, typhoid fever, and pyogenic infections. These were all cases which lived from several days to one and a half years after transfusion.

2. The second group of the cases which died consisted of 23 cases of some disease of itself so grave that transfusion could not have been expected to do much good, and was only resorted to as a desperate hope. These included cases of acute lymphatic leukemia (3 cases), typhoid perforation (1 case), brain tumor (1 case), diabetic coma (3 cases), uremia (1 case), hemorrhagic diphtheria (1 case).

3. The third group of fatal cases consisted of 23 patients in whom transfusion might have been expected to be beneficial, but actually did little or no good. Of these the most disappointing were 4 cases of postoperative shock and 6 cases of pathological hemorrhage (including 4 of cholemia and 2 of purpura hemorrhagica). In these instances, contrary to expectation, the hemorrhages were not influenced by transfusion. There were also 3 cases of hemorrhage in typhoid fever.

Finally, there were 2 cases (1 of pernicious anemia and 1 of subacute streptococcus endocarditis) in which the unfavorable outcome was hastened by transfusion of excessive amounts of blood and 3 cases in which the fatal result was probably due to transfusion of incompatible (agglutinative and hemolytic) blood.

Part II.

SPECIAL INDICATIONS.

These are subdivided according to the following scheme:

I. Transfusions for simple hemorrhage.
   1. Gastric and duodenal ulcer.
   2. Dysentery.
   3. Typhoid hemorrhage.
   4. Ectopic pregnancy.

II. Transfusions in connection with surgical operations.
   1. Preliminary to operation.
   2. For postoperative hemorrhage.
   3. For shock.

III. Transfusions for the cure of hemorrhagic conditions.
  1. Purpura hemorrhagica.
  2. Hemophilia.
  3. Hemorrhages secondary to
    (*a*) Blood diseases.
    (*b*) Severe infections.
    (*c*) Jaundice (cholemia).

IV. Transfusions for blood diseases.
  1. Pernicious anemia.
  2. Leukemia.

V. Transfusion for infections.
  1. Infections with pyogenic organisms.
  2. Subacute streptococcus endocarditis.

VI. Transfusions for intoxications.
  1. Acute poisoning.
  2. Diabetic coma.

VII. Transfusions for debilitated conditions.
  1. Cancer.
  2. Malnutrition.
  3. Simple anemia.

I. Transfusions for Simple Hemorrhage. 1. *Gastric and Duodenal Ulcer.* There were altogether 14 cases of gastric or duodenal ulcer transfused. Almost all of these were in desperate condition at the time the transfusion was done; 12 of the 14 recovered. The 2 deaths occurred not from a continuance of the hemorrhage but from peritonitis and other complications following the laparotomy. Of the 12 cases which recovered, 4 were cases of duodenal and 8 of gastric ulcer. In all the cases there was a severe anemia, and actual hemorrhage was still going on at the time of the transfusion.

The hemorrhage in these cases was slight at the time, probably due to exsanguination, and the transfusion seemed to exert a beneficial effect on the hemorrhage itself.

Of the 2 cases which died, 1 was a case of duodenal ulcer, 1 a case of multiple gastric ulcers complicated by a cholecystitis; 1 of these cases continued to bleed after the transfusion. Death in this case was not due to the bleeding, however, which was relatively slight, but to a general peritonitis following pylorectomy.

The results in the gastric and duodenal ulcers show that transfusion exerts an exceedingly favorable effect on hemorrhage. It should be said that the two fatalities in ulcer cases were among the three operated cases, but that in these three cases the operation had to be performed for other indications than hemorrhage.

There were 4 additional cases of severe gastro-intestinal hemorrhage not included in the list of gastric ulcers. Only 1 of these recovered. One was a patient who had been suffering from a chronic

anemia with a large spleen for a year or more, and who suddenly had a profuse gastric hemorrhage. A large transfusion was done, but the hemorrhage continued and the patient died within twelve hours. It seems likely that the hemorrhage may have been due to thrombosis of the splenic vein. Another was a case of profuse gastric hemorrhage secondary to cirrhosis of the liver; this case recovered. The third was a fatal case of postoperative gastric hemorrhage following extirpation of the rectum for carcinoma; and the fourth, a case of hemorrhage from a carcinoma of the stomach in which the patient died after a subsequent operation.

It is a striking fact that in almost all the cases of gastric or duodenal ulcer the hemorrhages stopped after transfusion. At first there was considerable hesitation about transfusing these cases during active hemorrhage on account of the danger of raising the blood-pressure and thus increasing the hemorrhage. This danger undoubtedly does exist, and because of it we would warn against transfusion in acute first hemorrhages (except for the purpose of saving the patient from immediate exsanguination).[7] *The cases in which transfusion seems actually to check hemorrhage are those of repeated or prolonged bleeding.* In these cases (as anyone who has tested the coagulation time of many patients has observed) the coagulation time of the blood is normal or even shortened, but the clots are of a flabby nature, different from the firm tough clots of chronic anemias. It seems likely that these soft clots form imperfect thrombi and thus the mere prolongation of a hemorrhage causes a vicious circle and tends toward its further prolongation. Transfusion checks the hemorrhage by supplying blood which can form normal thrombi.

The same explanation of the hemorrhage-checking effect of transfusion applies, of course, not only to gastro-intestinal, but to other forms of prolonged hemorrhage, and partly to the hemorrhagic diatheses.

2. *Dysentery.* There were transfusions in 6 cases of severe dysentery. These patients were all profoundly anemic, due not only to hemorrhage, but to nutritional disturbance. In all the cases the immediate results of the transfusions were very good, but in 4 of the 6, the intestinal disturbance continued and the patients ultimately died. In one of the patients the dysentery finally yielded to treatment and recovery ensued. In 1 the general condition was bettered, but the patient has continued to suffer from intestinal symptoms.

In severe dysentery, then, transfusion is worth trying as a temporizing measure.

3. *Typhoid Fever.* As the chief indication for transfusion in typhoid fever is usually hemorrhage, all the cases of typhoid fever

[7] Repeated small transfusions done by the newer methods would, however, be applicable (see Addendum).

will be summarized here. There were nine transfusions in 7 cases of typhoid fever. Of the 7 patients, all in the most desperate possible condition, 2 ultimately recovered. One of the fatal cases should perhaps be excluded, as it was a case of intestinal perforation in which transfusion was done in the hope of bringing the patient, already in profound shock, into a condition in which an operation could be done. The transfusion was without effect. The 6 other patients suffered from severe and protracted hemorrhage. In the 2 who recovered the hemorrhage practically ceased after the transfusion. Of the 4 who died, 3 had hemorrhages so large that transfusion could accomplish nothing. In the fourth the hemorrhages stopped for a time after transfusion only to begin again after a few days. Two weeks later a second transfusion again relieved the symptoms due to hemorrhage, and the bleeding stopped. The fever continued and the patient died three weeks later of exhaustion. If, as seems fair, we include the two transfusions in this case among those in which the symptoms of hemorrhage were relieved by transfusion, we can say that there were four such transfusions among the seven done for typhoid hemorrhage.

One of the 2 cases that recovered has been reported by Dr. Manges,[8] with whom we had the privilege of observing the patient. In this case two transfusions were done. After the first the hemorrhage ceased. There continued, however, a remarkably protracted and severe typhoid infection, and there developed a general streptococcus infection. A second transfusion was done a month after the first, and the patient recovered with surprising promptness.

As the two patients who recovered would in all probability have died without transfusion, it is undoubtedly a useful method in the treatment of severe typhoid fever. In the presence of exceedingly large hemorrhages it can have, of course, only a temporary stimulating value. In cases of protracted or repeated hemorrhage it not only replaces the lost blood, but may help check hemorrhage. (See above under Gastric Ulcer.) *In all typhoid cases the first appearance of blood in the stools should be an indication to make preparations so that a transfusion can be done, if needed, at very short notice.* If the transfusion is not needed, little is lost; if it is needed, invaluable time is gained. Finally, in the typhoid state and in very protracted cases of typhoid, transfusion may have life-saving value and should be tried oftener than it has been.

4. *Ectopic Pregnancy.* There is perhaps no single condition to which transfusion would seem to be more ideally suited than ruptured ectopic pregnancy. There were three such cases in our series, and in all of them the transfusion was life-saving. The circumstances of the transfusion in the three cases differed slightly.

[8] New York Med. Rec., 1912, lxxxi, 979.

The one was an emergency case, an almost exsanguinated patient, and a transfusion was done immediately after the operation. Another had been operated upon, but two days after the operation she was doing badly and a large transfusion was done. The third was a case which bled slowly and in which the diagnosis was at first not certain. A transfusion raised the hemoglobin from 25 to 50 per cent., and a successful laparotomy was performed two days later.

II. Transfusions in Connection with Surgical Operations. 1. *Preliminary to Operation.* Among the most satisfactory transfusions in the whole series were some of those done preliminary to an operation upon patients whose desperate condition would otherwise have contra-indicated any operation. There were 33 such preoperative transfusions and in 13 of them the result was decisive and the patients recovered. The actual effects of such transfusions are even better than these figures show, because a majority among those that died did so as a result of postoperative complications (such as peritonitis or pneumonia) or of a continuation of the original disease (such as metastatic carcinoma). Three died of operative shock; and our experiences have not led us to think that transfusion has any specific effect in preventing shock further than its effect in restoring to the patient more or less of his original power of resistance.

2. *For Postoperative Hemorrhage.* Little need be said about postoperative hemorrhage that has not been said about hemorrhage in general. Transfusion is the ideal remedy, but, of course, if the hemorrhage is not at the same time checked the ultimate outcome will not be affected. There were 5 transfusions for hemorrhage after operation (not including the transfusions for postoperative hemorrhage due to cholemia, which will be discussed separately). In 3 of the cases there were brilliant recoveries, in 2 death. In the 2 fatal cases (nephrotomy and operation for malunion of fractured femur) shock probably played almost as large a role as hemorrhage. (In the former of them transfusion of incompatible blood may have been a contributing factor.[9])

3. *For Shock.* There were seven transfusions for postoperative shock. All the patients died within an hour to five days, and it seems probable that transfusion is not to be relied upon clinically as a remedy for pure shock. In four of the cases (nephrectomy, bone-plating, prostatectomy, amputation of leg) hemorrhage played an important but secondary role. The results are the more disappointing as shock is one of the conditions in which it was at first thought, from the experimental work of Crile and his collaborators, that transfusion would be life-saving. This much, however, is to be said about our results: the transfusions were all done late,

[9] See below under Dangers of Transfusion.

after the shock had lasted for some hours to several days. It is possible that if the condition of shock could have been foreseen and transfusion done immediately after the operation instead of after many hours of delay the results (especially in those cases combined with hemorrhage) might have been better.

III. Transfusions for the Cure of Hemorrhagic Conditions. The group of hemorrhagic diseases is a heterogeneous one comprising a number of conditions of very diverse pathogenesis. For practical purposes the 35 cases in our series can be grouped under (1) idiopathic purpura hemorrhagica, (2) hemophilia, and (3) secondary hemorrhagic disease complicating such conditions as severe infections, pernicious anemia, leukemia, and prolonged jaundice. Of hemorrhagic disease of the newborn, which has proved so brilliant a field for transfusion therapy, there was only one case in our series, and as the disease in this case was probably secondary to a staphylococcus infection, it will be included under the heading of secondary hemorrhagic disease.

1. *Purpura Hemorrhagica.* Idiopathic purpura hemorrhagica is characterized by the occurrence of spontaneous hemorrhages in various locations. The number of blood platelets is usually decreased greatly, but the coagulation of the blood is generally unimpaired. These two laboratory criteria were sought for and found in most of the cases of our series. The milder purpuras, as a rule, recover spontaneously. The more severe ones are frequently fatal, and it is only in this class of severe purpuras that transfusion is often used.

There were twelve transfusions in 9 such cases of severe purpura. Of the 9 cases, 2 died, uninfluenced except as to temporary replenishment of blood, 6 recovered completely, and 1 left the hospital improved. More striking than the statistics (especially in a disease of which the milder cases usually recover) was the prompt cessation of hemorrhages in most of the cases. This phenomenon leaves little doubt that beside the effect of transfusion in replacing lost blood, it has a definite curative value in these cases. On what the curative value depends is at present not at all clear. It is evidently not due to restored coagulability of blood (as it is in hemophilia), for in purpura the blood clots normally. That it has some connection with the fresh supply of blood platelets seems likely. Platelets have been shown to possess an important function in thrombus formation quite apart from their role in mere blood coagulation. But the normal life duration of platelets is known to be very short, and it does not seem probable that the relatively limited supply of platelets, even in a large transfusion, can account for all the benefit produced.

Of the 9 cases, the 2 which were fatal form a peculiar group, because they were both cases of postpartum purpura hemorrhagica. In both cases the hemorrhages were entirely uninfluenced by rather

large transfusions. It is possible that the pathogenesis of these cases is different from that of the others.

Of the 7 cases which recovered all were in desperate condition at the time of transfusion, in 6 of them the hemoglobin being reduced to between 10 and 25 per cent., and in the seventh, to 42 per cent. In 4 of these cases the cessation of hemorrhages was prompt and complete after transfusion. (In 1, however, a case with ecchymoses, hemorrhages from the gums and profuse uterine hemorrhage, the uterine hemorrhage recurred after four months. A hysterectomy was done and the patient recovered, and according to the notes supplied us by Dr. Maybaum the patient has remained well for seven months.) In the other 3 cases the cessation of hemorrhage after transfusion was not complete; slight subsequent hemorrhages did occur, but the turn for the better was unmistakable; 2 of them ultimately recovered completely; the third, in spite of three transfusions, was still suffering from purpura when she left the hospital after three months.

In all of these cases, before transfusion was resorted to, attempts were made to check hemorrhage by serum treatment—subcutaneous, intravenous, or local use of human, horse, or rabbit serum—and entirely without effect. We will return to the subject of serum treatment under the heading of hemophilia.

2. *Hemophilia.* This disease is one in which transfusion may fairly be spoken of as specific therapy for the control of hemorrhages. The exact pathogenesis of the hemorrhages is not entirely understood, but what we do know throws considerable light on the mode of action of the transfused blood. When blood is obtained from the vein of a hemophiliac during an interval between hemorrhages, the coagulation time is enormously prolonged but the clot which finally forms is normal in texture and amount. Analysis shows that the delayed coagulation is due to deficiency in some element that goes to form thrombin (fibrin ferment). Experimenters are not all agreed as to which element is lacking, but the preponderance of evidence favors the view that the power of producing the activating substance (known under a variety of names—thrombokinase, thromboplastin, cytozyme) is diminished in the circulating blood. On the other hand (and this is a very striking fact) there is evidence that this activating substance is not lacking in the tissue cells. And this corresponds to the well-known clinical fact (confirmed by us in a number of cases) that in hemophilia, even when blood obtained directly by venipuncture shows greatly prolonged coagulation time, blood obtained from small cuts or pricks, clots in approximately normal time. It is clear that transfusion stops hemorrhage in hemophilia by supplying the patient's blood with the lacking element; and it is also clear (*a priori* as well as from our clinical experience) that such cures are not permanent, that sooner or later the fresh supply of thrombin-forming substance

must become exhausted and the tendency to hemorrhage exist anew.

There were five hemophilia cases in our series. All were males; four were children. Three gave typical family histories. The fifth case was a boy of sixteen and no family history of bleeding could be obtained, but the hemophilia had existed from birth.

The first case was not anemic but had a history of repeated hemorrhages from various sources, and was admitted to the hospital with hemorrhages into several joints. After the transfusion there were no further hemorrhages, and the patient left the hospital in good condition. He reëntered the hospital three months later with renewed hemorrhages into the joints and from a small wound. The second case was a brilliant cure, the child being almost completely exsanguinated before the transfusion. No further hemorrhages occurred after the transfusion. In the third case, in spite of a successful transfusion, bleeding from a small wound in the chin stopped for only twenty-four hours after transfusion. The patient was taken home against advice and lost track of. The fourth case was a child with protracted hemorrhage from a cut in the mouth. Bleeding stopped at once after an intravenous injection of 25 c.c. of whole blood from the father. The fifth case was a boy aged sixteen years, who had since birth had repeated hemorrhages from various parts of the body, and who twice underwent probably life-saving transfusions when almost exsanguinated. In each instance hemorrhage stopped at once after transfusion.

Including the two transfusions in the fifth case, we can then report six transfusions in hemophilia cases. In all but 1 of the cases the transfusion was only done after protracted hemorrhage had failed to yield to all other kinds of treatment, including serum treatment. In five out of the six transfusions the hemorrhage was checked promptly and the patients regained good health. In the 2 cases that could be followed for some time the tendency to hemorrhage reappeared after weeks or months.

Hemophilia is a disease with a high mortality. The majority of persons afflicted with it never reach adult life. (This is what has given rise to the erroneous statement that the disease is only transmitted by females.) Transfusion, it seems to us, offers a new hope for these doomed individuals, and we would suggest the following plan of procedure:

Every individual known to have hemophilia ought to have at his command several persons whose blood by previous tests[10] *is*

[10] Such tests, once performed, would not need to be repeated when the transfusion is done, since the agglutinative property of the blood of certain individuals for the blood cells of certain others are permanent for life, and the hemolytic property which occasionally occurs develops, as a rule, only where there is already agglutinative power present. However, if transfusions are repeated the tests should be repeated also, as we know from experimental work (Ottenberg, Kaliski, and Friedman, loc. cit.) that it is possible to develop immune isohemolysins by repeated direct transfusions.

known to be compatible with his, and who are willing, when called upon, to give blood for transfusion. These donors, if relatives of the patient, should have the possible existence of latent hemophilia excluded by blood tests as well as by consideration of the hereditary laws of the disease. Whenever serious hemorrhages occur, prompt transfusion should be done, preferably by the syringe method, as this does not injure the vein, and hence allows for any number of future transfusions. It seems to us possible that by this system the majority of hemophiliacs might be enabled to lead a life of normal duration.

It seems to us, further, that in these cases the prophylactic effect of small transfusions (25 to 50 c.c.) repeated at long intervals (one to three months) would be well worth trying. Such injections of one or two syringefuls of unaltered blood could easily be performed as an office procedure by any one skilled in the syringe method.

Comparison of Transfusion with Serum Treatment. Almost all the hemorrhagic cases (including those to be described below) and a number of the cases of hemorrhage from other causes (such as typhoid ulceration and gastric ulcer) received subcutaneous or intravenous injections of fresh serum before transfusion was resorted to. Without going into details we believe we can say that the serum treatment was given a fair trial; the serum was used in large amounts and repeatedly. We have also had a considerable experience with serum treatment in cases which did not come to transfusion. In spite of the occasional cessation of hemorrhages after such serum injections we have not been able to convince ourselves that serum injections have any effect on hemorrhage. In 2 hemophilia cases (not transfused) the coagulation time was no shorter after than before serum injections (subcutaneous in one case, intravenous in the other).[11] On the other hand, we have often seen serum or defibrinated normal blood show an unmistakable effect in stopping hemorrhage when applied directly to small bleeding points.

The rationale of serum treatment and of transfusion for hemorrhagic conditions is indeed different. The active ingredient of serum is thrombin (fibrin ferment). Thrombin never exists in circulating blood but is formed only when blood is shed. When injected into the circulation it is at once neutralized by the antithrombin which exists in blood plasma. If it were not so neutralized it would cause intravascular clotting. Serum, therefore, cannot be expected to exert any thrombin action at a bleeding point distant from the point of injection. Whatever distant effect it has is probably in the easily assimilable nutrition which it offers, or possibly the

[11] It is of interest to note that we once saw bleeding stop (case of carcinoma of pancreas, icterus, general hemorrhages) following the use of serum, although the coagulation time became much longer. The coagulation time is not, therefore, always an index of the bleeding tendency.

serum ingredients can be made over by the body into the predecessors of thrombin. Transfusion of whole blood, on the other hand, supplies the body at once with all the substances in plasma, cells and platelets necessary to elaborate thrombin at a distant bleeding point.

Nevertheless, on account of the favorable reports of others, and particularly on account of the successes reported in hemorrhagic disease of the newborn (a condition with which we have had little experience), we believe that serum treatment deserves a further clinical trial.

2. *Secondary (symptomatic) Hemorrhagic Disease.* Hemorrhagic disease is frequently secondary to some other condition, such as severe infectious diseases, blood diseases (leukemia, pernicious anemia), and intoxications (nephritis, jaundice, etc.). It seems probable too that further study will show that many of the cases now classed as idiopathic are really secondary. There were 18 undoubtedly symptomatic cases in our series, 3 secondary to infections, 5 to leukemia, 1 to pernicious anemia, 8 to cholemia (prolonged jaundice), 1 to nephritis.

The pathogenesis of the hemorrhages in these secondary cases is variable, as Whipple and others have shown. In some, deficiency in fibrinogen, in others a lack of some of the ferment-forming substances, and in still others an excess of antithrombin have been demonstrated. Whatever the pathogenesis, however, the transfusion of blood would seem to be a logical procedure.

(*a*) *Secondary to Severe Infections.* There were three such cases. The first was a case of hemorrhagic disease of the newborn in a child whose mother had breast abscesses. The immediate result of the transfusion was brilliant. The hemorrhages stopped at once and the temperature dropped. After the transfusion, however, the temperature gradually rose again, ear suppuration set in and bleeding recurred from the mouth, skin, and intestines. The hemorrhages now were very slight and the child died of infection, not of hemorrhage.[12]

The second was a case of gonorrheal rheumatism with very severe hemorrhagic disease. The blood culture was negative, and it is not absolutely certain that the purpura was secondary to the gonorrhea. The patient's general condition which had been steadily getting worse before the transfusion, commenced to improve almost at once after it. There continued, however, to be some new hemorrhages, joint pains, etc., for about a week. The general clinical course of the disease was abruptly changed by the transfusion, and the patient ultimately recovered.

The third was a case of hemorrhagic diphtheria.[13] After the

[12] This case is fully described by Schwartz and Ottenberg, AMER. JOUR. MED. SCI., 1910, cxl, 17.

[13] We are indebted to Dr. Louis Fisher for permission to refer to this case.

transfusion the bleeding from the nose stopped and petechiæ no longer appeared, but the toxic symptoms due to the diphtheria continued, and the patient died one week later.

It is apparent, then, that in hemorrhages secondary to infections transfusion may check the hemorrhage, but that, of course, the ultimate result will depend upon whether the body overcomes the infection.

(*b*) *Secondary to Leukemia or Pernicious Anemia.* The results in leukemia in general will be discussed below, but there were 4 cases of lymphatic leukemia in which the indication for transfusion was hemorrhage from the mucous membranes. In 3 of these cases the leukemia was acute and the hemorrhages were uninfluenced by transfusion. In the fourth case the leukemia was of the chronic type, and the hemorrhages, which had not been so severe as in the other 3 cases, stopped after transfusion.

The case of pernicious anemia was one in which the hemorrhagic tendency only appeared when the leukopenia became marked (between 950 and 3000 leukocytes per cubic millimeter). Transfusion had little effect.

Aside from these cases it is possible that a peculiar form of purpura fulminans in which the polynuclear leukocytes are so greatly diminished as to almost disappear while the lymphocytes in the blood remain approximately normal or increase, is really a form of sublymphemic leukemia (perhaps better called leukopenic lymphemia). We have observed several such cases. One of them was one of the fatal cases described above under the heading of Idiopathic Purpura.

(*c*) *Secondary to Jaundice.* There were thirteen transfusions in 12 cases of prolonged obstructive jaundice. Of these cases 4 were transfused preliminary to operation to prevent hemorrhage, 7 were transfused for persistent hemorrhage after operation, and 1 was transfused simply to improve the general condition. Of the 4 cases transfused to prevent postoperative hemorrhage, such hemorrhage occurred, nevertheless, in 1. In this case a fatal intraperitoneal hemorrhage took place. Of the others, 1 died three days after laparotomy with symptoms of cholemia; the third stood the exploratory laparotomy well and died three months later. All of the 3 cases proved at the operation or autopsy to be cases of malignant disease.

The fourth case of transfusion preliminary to operation was a case of obstructive jaundice due to stone in the common duct, in which hemorrhages from the intestine leading to a marked anemia occurred before any operation was attempted. No further hemorrhages occurred after transfusion, and a successful operation was done. This was the only case in the twelve transfused for jaundice, which ultimately recovered.

Of the 7 cases of obstructive jaundice with persistent postopera-

tive hemorrhage, 4 were due to stone or inflammation, 3 were cases of malignant disease. In all 4 of the non-malignant cases, hemorrhage from the wound continued after the transfusion as before.[14] Of the 3 malignant cases, 1 was improved by the transfusion. There were no further hemorrhages, and the patient left the hospital relieved. The second was a case in which there was an almost fatal hemorrhage from the gums and the wound two weeks after operation, with repeated small hemorrhages continuing. Transfusion, only done a month after the operation, greatly improved the patient's general condition. Repeated small hemorrhages continued, but the patient lived for three months after transfusion. In the third case gastric hemorrhage continued unchecked by the transfusion and the patient died.

Postoperative hemorrhage due to cholemia was checked then completely in only 1 case, partly in 1 other, and not at all in 5 cases. Furthermore, the precautionary transfusion before operation failed to prevent the dreaded postoperative hemorrhage in 1 of the 4 cases in which it was tried. These results are disappointing and require explanation.

The exact cause of the hemorrhagic tendency in jaundice is still a matter of dispute, but undoubtedly the changes in the viscera as well as in the blood resulting from the prolonged toxic action must be profound. One can hardly expect these changes to stop at once even after successful operation; and it would seem that the value of the transfused blood is impaired by the same toxic agencies which have already injured the patient's blood. If better results are to be obtained in these cases we shall probably have to adopt the rather bold course of a preliminary blood-letting followed by a large transfusion (two donors), so as to replace as much as possible of the patient's blood. If this is not done before operation, preparations should be made before operation so that in case of hemorrhage it can be done at the earliest moment. And finally transfusions should be repeated, if necessary.

IV. Transfusions for Blood Diseases. 1. *Pernicious Anemia.* There is no question connected with transfusion that has aroused more interest than that of the value of transfusion in pernicious anemia. The experiences of different observers have varied widely; while some have reported brilliant results others have condemned transfusion as useless or even harmful. With an experience of thirty-five transfusions in 25 cases of undoubted pernicious anemia we have been able to reach certain definite conclusions. (We are excluding from consideration 3 cases in which the diagnosis of pernicious anemia was not certain, 2 of which made apparent cures).

In the 25 definite cases there were no cures; 14 of them under-

[14] One of these cases was transfused twice; in this case the serum of the donor was agglutinative to the patient's blood cells.

went more or less prolonged remissions immediately following transfusion, while 11 of them showed little or no effect.

Of the 11 which showed little effect, 3 were moribund at the time of transfusion and died within a few hours or days. The other 8, in spite of marked rise of hemoglobin and temporary symptomatic improvement, showed no interruption in the course of the disease but continued to destroy their blood at about the same rate as before transfusion.

Of the 14 patients who showed progressive improvement following one or more transfusions, 1 had a remission lasting approximately three months, 3 had remissions lasting six or more months, 3 lasting a year or more, and 3 lasting over two years; 8 of the patients are alive, 3 of them less than three months, the others respectively six months, nine months, one and a half years, two and three-quarter years, and four years since the first transfusion. Of these all are in a remission stage. We believe that our results would have been still better had we been in a position to have the transfusions repeated whenever the hemoglobin began to drop.

Two patients underwent splenectomy subsequent to transfusion. In one of these the splenectomy was done after the patient had left our hands, and we only know that in general the splenectomy had little effect and the patient died a few months after it. The second was a remarkable case, already reported by Dr. Buerger.[15] In this case the first transfusion done over three years ago, at a time when the patient seemed in an almost hopeless condition (hemoglobin 18 per cent., general anasarca), was followed by a remission lasting a year, during which the patient was practically in perfect health but showed the blood picture typical of pernicious anemia remissions. Then the anemia gradually progressed again, and a year and a half after the first a second transfusion was done. The patient only held this blood for a few weeks and then again gradually became anemic, so that after three months the hemoglobin was 26 per cent. A third transfusion now raised the hemoglobin to 35 per cent., and a week later, when the hemoglobin had risen to 53 per cent., a splenectomy was done.

Since the splenectomy, the patient has been in a remission stage and she is now in excellent health. The examination of the blood on March 15, 1915, showed the following: Hemoglobin, 102 per cent.; erythrocytes, 3,660,000; leukocytes 9500; polynuclear neutrophiles, 53 per cent.; lymphocytes, 43 per cent.; mononuclears, 2 per cent.; eosinophiles, 2 per cent.; no nucleated erythrocytes or Jolly bodies;[16] undoubted tendency to macrocytosis.

Transfusion, then, so far as our experience goes, is never curative in pernicious anemia. It is a symptomatic remedy which with greater certainty than any other known remedy overcomes the chief

[15] New York Surg. Soc., October 2, 1914.

[16] Jolly bodies had, however, been present for a long time after splenectomy.

symptom of the disease—the anemia. But it does more than this; in about half the cases it initiates a remission. It is true that remissions occur even in the most desperate-seeming cases without transfusion. But the promptness with which the remission occurred in 14 of our cases leaves no doubt that the transfusion stimulated the remission.

It is well known, of course, that cases of pernicious anemia often pass early in the disease through one or two blood crises in which marked anemia is followed by a striking remission. And it might be thought that those cases in which transfusion was followed by a remission were such early cases, and that the transfusion merely coincided with the blood crisis. But an investigation of the histories of the cases shows exactly the opposite to have been the case. The cases which improved after transfusion were mostly cases which had already run a rather long course and gone through one or two crises, while the cases which failed to improve were for the most part cases of short duration. Of 12 cases whose previous histories could be fairly accurately ascertained and which showed remissions after transfusion, the average duration of the disease before transfusion was nineteen months, whereas of 8 similar cases which failed to show a remission the average previous duration was only ten months (Table I).

TABLE I.—Duration Before Transfusion of Cases in Which Transfusion was Followed by

Remission.		No remission.	
Case No. O. S. 18	3 years.	Case No. O. S. 53	6 months.
" No. O. S. 43	3 years.	" No. O. S. 60	6 months.
" No. O. S. 87	3 months.	" No. O. S. 85	6 months.
" No. N. S. 1	1½ years.	" No. N. S. 35	2 years.
" No. N. S. 9	8 months.	" No. N. S. 53	9 months.
" No. N. S. 22	2 years.	" No. N. S. 54	3 months.
" No. N. S. 42	2 years.	" No. N. S. 78	2 months.
" No. N. S. 66	6 months.	" No. N. S. 99	2 years.
" No. N. S. 83	1 year.	(First transfusion.)	
" No. N. S. 91	1 year.		
" No. N. S. 93	3 years.		
" No. N. S. 99	2 years.		
(Second transfusion.)			

From this we can roughly divide pernicious anemia cases into two groups: (1) chronic cases which tend to undergo remissions spontaneously and in which new remissions can be brought about by transfusion, and (2) virulent, rapidly progressive cases in which transfusion has little effect.

Aside from this we cannot say what factors determine whether a given transfusion will produce a remission or not. The size of the transfusion is not the deciding factor because remissions occurred after small as well as after large transfusions. Compatibility of the blood, in the ordinary sense, plays no role, as hemolysis and agglutination were most carefully excluded in all but 1 of our

cases (this case died eight hours after transfusion). There are probably other not yet recognized differences between the bloods of donors, and we would suggest that if a remission occurs after a first transfusion an effort be made to obtain the same donor when another transfusion becomes necessary for the patient, whereas if no remission occurs a different donor ought to be tried. *In 2 of our cases in which a first transfusion failed to produce a remission a second transfusion from a different donor did so.*

It is possible that the degree of anemia which is reached before transfusion is resorted to may have something to do with determining a remission. The average hemoglobin percentage, before transfusion, of the 14 cases which showed remissions was 27 per cent., whereas the average of 9 cases which showed no remissions (excluding the 3 rapidly fatal cases) was only 20 per cent. In the former group there were 6 cases with hemoglobin of 30 per cent. or over, while in the latter there were only 2 cases in which the hemoglobin was as high as 30 per cent. This is, however, not an invariable rule, as 4 of the remission cases had low percentages (10, 13, 15, and 16 per cent. respectively) before transfusion. This observation should, nevertheless, certainly lead us to abandon our present timid habit of waiting until an extreme grade of anemia is reached before transfusing these cases.

This conclusion is further supported by another consideration. Anemia itself leads to disturbed functions or actual degenerations of viscera. Thus the persistence of a grave anemia hinders recovery from any disease, including anemia, while the mere temporary relief of anemia tends to break the vicious circle.

The effect of the transfusion on the general condition of patients with pernicious anemia is very often striking. The appetite usually improves rapidly and mental disturbances are apt to clear up. As far as our experience goes the glossitis is not directly influenced nor are, as a rule, the symptoms indicative of spinal cord involvement (except as regards the feeling of weakness which may improve with the increased feeling of strength in the entire body). In 2 cases in which we studied the gastric secretion after transfusion the achylia persisted, although the appetite and the subjective gastric symptoms improved greatly. In our last case we found that the systolic murmurs heard over the heart disappeared when the remission following transfusion was well established.

Of particular interest is the influence of transfusion on the fever, which is such a conspicuous feature of a large number of cases of pernicious anemia. It has been found in over 60 per cent. of the cases (in one report as high as 80). In 5 of the 6 febrile cases which we investigated the fever disappeared after transfusion. This phenomenon is not peculiar to this form of anemia, for among 16 other cases of anemia due to a variety of causes (excluding infections), febrile before transfusion, 8 became afebrile after it. (These

included cases of gastric hemorrhage, hemophilia, splenomegaly, uterine hemorrhage, purpura, etc.). These observations lend strong support to the view that there exists a fever dependent upon anemia as such, the so-called "anemic fever."

We have in transfusion a means of determining in pernicious anemia (and probably in some other conditions) which symptoms are due to the poison of the disease and which to the anemia that is one of the results of the poison.

We may summarize our conclusions with regard to pernicious anemia as follows: *Transfusion is the best remedy for pernicious anemia; it never cures, but it leads to remissions in about half the cases;* it may repeatedly lead to remissions, but the duration of the later remissions is usually shorter than of the early ones. This is possibly due to the mere exhausting effects of protracted anemia itself. For this reason we believe that transfusion should be resorted to early instead of late, and that it should be persistently repeated as often as is necessary to keep the patient from developing a marked grade of anemia.

With regard to splenectomy, we believe from the experience up to the present time that it should be done when remissions of good duration are no longer (or not at all) obtained by means of transfusion. It may, of course, be necessary to transfuse before splenectomy if the patient is in a precarious condition. It is advisable that in patients who have been splenectomized and have had no remission, or who relapse, transfusions be tried. In this way we will learn whether the patient's life is more prolonged by initial splenectomy and later transfusions, or *vice versa*.

2. *Leukemia.* There were transfusions in 10 cases of leukemia, 9 of the lymphatic, 1 of the myeloid type; 4 of the cases were of the acute variety, with large lymphocytes predominating. In 3 of these the transfusions were without effect and the patients died in a few days. In the fourth the patient's life was probably prolonged for three months by two transfusions. In these cases there were no significant changes in the blood-picture following transfusion.

Of the 5 cases of chronic lymphatic leukemia 1 showed little change in the blood or in the clinical condition the other 4 showed along with some clinical improvement interesting changes in the blood-picture.

The first case was remarkable. It was a typical case of chronic lymphatic leukemia of a year's duration, showing, besides enlargement of the spleen and lymph nodes, peculiar skin infiltrations. The white cells numbered 120,000 and the lymphocytes 85 per cent. Simultaneous with transfusion a phlebotomy of fifty-five ounces was performed by Dr. Harold Neuhof (to whom we are indebted for the use of his notes). A month after transfusion the leukocytic blood count had become practically normal, and it remained so

until the patient's death, one year later. The skin infiltrations, splenic and lymph-node enlargements, diminished for about two months, then returned, and the skin lesions developed into large tumors of the appearance of mycosis fungoides (a condition which resembles leukemic cutaneous lesions). These progressed and caused death. We are at a loss to explain the permanent change in the blood picture; it could hardly have been due to the Roentgen-ray treatment which was given from time to time.

The other 3 cases also showed marked change toward the normal, or for a time actually normal leukocytic blood pictures, but in all of them the leukemic blood picture ultimately returned. In the second case this change was least marked; the leukocytes, which had been 10,000 with 5 per cent. polynuclear cells and 95 per cent. lymphocytes before transfusion, became 4,500, with 30 per cent. polynuclears the next day, but in a week had returned to about the same as before transfusion.

The third patient showed a gradual change. Two days after transfusion the leukocytes had decreased from 140,000 to 66,000 and the polynuclears increased from 18 to 35 per cent. This steadily progressed until two and a half months later, when the total and differential leukocyte count was entirely normal. During this time the treatment carried on by Dr. Alfred Meyer, consisted of frequent intramuscular injections of ascitic fluid. The leukocytic blood picture remained normal (in spite of progressing anemia) for another month; then the leukemic blood type gradually returned and the patient died four and a half months after transfusion.

In the fourth case an extreme leukemic blood-picture gradually became normal a week after transfusion (concomitant with striking clinical improvement). The leukocyte picture persisted normal for a week, and then in a few days became typically leukemic again. In the one case of myeloid leukemia there was no effect on either blood picture or clinical course.

Contrary to our expectation we find, then, that transfusion does exert an influence on chronic lymphatic leukemia. The blood counts in these cases were repeatedly made, and were confirmed by several men, so that there is no possibility of error. It is true that the patients were receiving the other usual forms of treatment, but so were they before transfusion; and everyone knows how rare it is for cases of lymphatic leukemia to get a quantitatively and qualitatively normal leukocyte picture under treatment. In one of the 4 cases which showed a change it was transient and partial, and appeared immediately after transfusion. In the other 3 it appeared gradually during one or more weeks after transfusion and lasted one week in 1 case, about two months in another, and a year (until death) in a third.

It should be remembered that all these cases received only one transfusion, and that the greatest result was obtained in the case

which had a rather large phlebotomy simultaneous with transfusion. We believe, therefore, that in some obscure way normal blood has an effect, and that the results of transfusion are good enough to warrant its further trial in chronic lymphatic leukemia. Such a trial should consist not of single but of systematically repeated transfusions, and we would suggest a preliminary or simultaneous phlebotomy as was done by Dr. Neuhof in his case.

V. Transfusions for Infectious Diseases. The idea of transfusion for infectious disease is almost as old as transfusion itself. Aside from the control of hemorrhage (in those cases complicated by hemorrhages), transfusion may be of use in infections, either for its general strengthening effect (particularly in protracted cases) or for some specific effect of the transfused blood. Normal blood usually has less specific bactericidal power than the blood of the infected individual, and for this reason the transfusion of normal blood probably helps only in the former way (general support). But the blood of persons who have recovered from an infectious disease or who have been artificially immunized has specific properties not only in the antibodies of the plasma but possibly also in the cells. For there is every reason to believe that in those diseases immunity to which is cellular rather than humoral the blood cells share the immune powers of the other body cells. And in this regard human blood offers the great advantage over animals' immune sera—that the blood cells transfused continue to live and functionate. Not enough attention has been paid to this possibility. We have made a small beginning in attempting to immunize a donor to the endocarditis coccus (Streptococcus viridans or mitis) before transfusion; but unfortunately most of the transfusions which we can report in infections represent haphazard trials in forlorn cases. Systematic attempts in this direction may be richly rewarded. Particularly in those diseases recovery from which confers lasting immunity, like typhoid fever, scarlet fever, and the other exanthemata, hospitals should endeavor to secure the consent of recovered patients to return and act as donors.

Aside from the typhoid fever cases (discussed above under hemorrhage in typhoid fever, and the cases of purpura complicating infectious diseases (discussed under Hemorrhagic Conditions, page 49), we can report on transfusions in 10 cases of infection with pyogenic organisms and in 4 cases of subacute streptococcus endocarditis.

1. *Infection with Pyogenic Organisms.* Of the 10 cases, 6 were due to the Staphylococcus aureus, 2 to general infection by streptococci, and in 2 the infecting organisms were not determined. All were in the most desperate possible condition at the time of transfusion, and the 4 that recovered probably owe their recovery to the transfusion.

The 2 cases in which the organisms were not ascertained were

both uterine infections, the one an infected abortion, the other a case of multiple infections (so-called pyemia) following a pelvic abscess. In both transfusion had no effect.

Of the 6 cases due to the Staphylococcus aureus, 4 were cases of osteomyelitis of the femur; 2 of these recovered; 2 were cases of multiple infections (pyemia) with bone abscesses, and 1 of these recovered. All 6 cases had been ill for two months or more and were very anemic (all but 1 had a hemoglobin percentage of approximately 30 per cent.). The 3 cases that died succumbed a few days after transfusion, and indeed were moribund at the time; 1 of them died of acute hemorrhage from an eroded artery. Of the 3 cases that recovered, all had been steadily growing worse before transfusion and promptly commenced to get well after it. The effect was unmistakable, and leaves no doubt that in prolonged suppuration mere anemia and exhaustion may be all that prevent the overcoming of infection. In such cases transfusion of normal blood may offer an almost specific cure.

Of the 2 cases of general streptococcus infection, the 1 which died was practically hopeless from the start, a Ludwig's angina with multiple abscesses, complicating diabetes. The 1 which recovered was a case of (apparently) terminal streptococcus blood invasion from an unknown source, complicating a remarkably prolonged typhoid fever. (This case has already been referred to under the heading of Typhoid Fever.) In this case also it was the mere exhaustion due to prolonged fever that allowed the secondary invader to enter the blood, and the recovery after transfusion was prompt and complete.

In prolonged infection, then (due attention having been paid to surgical needs), the transfusion of normal blood may be extremely valuable and should not be too long delayed. In acute infections the value of transfusion should be determined by more extensive studies than have hitherto been made.

2. *Endocarditis.* There were transfusions in 4 cases of subacute endocarditis due to the endocarditis coccus (Streptococcus viridans, Streptococcus mitis), 1 case being in the bacteria-free stage.[17] In the 3 active cases the transfusions were done in the hope of combating the anemia and of helping the patient fight the infection. In the bacteria-free case the object was the relief of a profound anemia.

In the first case two transfusions were done. At the time the first was done the hemoglobin was 39 per cent. The hemoglobin was raised to 55 per cent. and the next day was somewhat over 60. The general condition improved remarkably, but the temperature kept up as before, and the cocci were found in the blood repeatedly. The hemoglobin did not drop to the original figure for four months,

[17] Libman, Amer Jour. Med. Sci., 1913, cxlvi, 625.

a remarkable result, because in such cases, when not transfused, once the anemia begins it becomes progressive. A second transfusion was done, using a donor who had been treated with a vaccine made from the organism present in the blood of the patient. This transfusion relieved the anemia, but the patient died a short time later from cerebral symptoms interpreted as being due to the rupture of an embolic aneurysm.

There were two further observations made in this case that are of sufficient importance to mention here. Bactericidal studies were made of the serum of the patient and of the serum of the second donor. They were both moderately bactericidal, as was the mixture of the two. The full blood of each was also moderately bactericidal, but the combination of both full bloods was completely bactericidal. This shows that serum studies are insufficient. One should also study the plasma and the full blood if one wishes to obtain correct estimates in making bactericidal studies.

The other observation relates to a severe pain that the patient referred to the right orbit, and which disappeared promptly after the first transfusion. It did not return until the hemoglobin again was reduced to the early low figure. We were evidently dealing with an anemic neuralgia. This observation is, as far as we know, unique.

In the second case there was some improvement in the general condition, but only for a few days. The case was a very advanced one.

The third case was the only case in our entire series of a fatal accident following transfusion (aside from the two agglutinative and hemolytic transfusions discussed elsewhere[18]). A large transfusion was done and no track was kept of the hemoglobin (it was one of the early cases). At the end of the transfusion the patient suddenly showed all the signs of acute cardiac dilatation, and died a few hours later. Autopsy revealed not only extensive aortic and mitral vegetations and an unexpected tuberculosis of the lungs, but extensive miliary necroses of the heart muscle. It has never been entirely clear whether death was due to liberation of toxic substances by some lytic action of the introduced blood on the circulating bacteria or to mere mechanical dilatation of the already damaged heart muscle. The latter possibility, however, seems far more likely. Excessive transfusion is an accident which can now be easily avoided by the method of calculation which we have introduced[19] even when the transfusion is a direct one (artery to vein). Particularly in cases of cardiac disease should the amount to be transfused be carefully calculated.

The fourth case of endocarditis to be transfused was a man who had for some time been in the bacteria-free stage of the disease

[18] Ottenberg and Kaliski, loc. cit.

[19] Libman and Ottenberg, Jour. Amer. Med. Assoc., 1914, lxx, 764.

and who was suffering from anemia. The hemoglobin was 20 per cent., and the patient showed moderate general edema and marked edema of the feet and legs. He was put on the Karrel diet for a couple of days so that the addition of the transfused blood should not overburden his heart. The change in his condition after transfusion was very pronounced. Before the transfusion he had no appetite, suffered from insomnia, and had marked dyspnea even when walking on the level. After the transfusion his appetite returned, he slept well, felt much stronger, and was able to walk up four flights of stairs with only moderate discomfort. His dyspnea on exertion had evidently been due much more to his anemia than to his valvular disease. He eventually became anemic again and succumbed to his disease.

As to the advisability of performing transfusions in these endocarditis cases, we believe that they are worth trying so as to help keep the patient alive for a longer time, and so as to put the organs into better condition to respond to any methods of therapy that are tried. We believe in such cases it is advisable to test the value of repeated transfusions, especially because we now know that there is a tendency for them to become spontaneously bacteria-free.

VI. Transfusions for Intoxications. 1. *Acute Poisoning.* In severe intoxications transfusion would only seem to be indicated if a considerable part of the poison is contained in or has acted on the blood. Among poisons which act in this way are carbon monoxide, hydrocyanic acid, benzol, nitrobenzol, and possibly carbolic acid. In such cases, of course, a large phlebotomy must be done before or during the transfusion.

In illuminating gas poisoning, transfusion is now accepted as the best treatment. We have seen 1 case of poisoning by illuminating gas combined with a large dose of morphin. In this case the patient recovered after the letting of a pint of blood, a large transfusion, and artificial respiration for about three hours (part of the time by Meltzer's intratracheal insufflation).

In a case of poisoning by a large dose of morphin with an unknown but probably small dose of prussic acid the same measures failed to save the patient. However, he did have a temporary return of consciousness after (although not immediately after) transfusion.

2. *Diabetic Coma.* Four cases of diabetes were transfused. The idea of trying transfusion for the relief of diabetic coma occurred to Dr. Elsberg, and the first case was transfused by him. Temporary improvement of an impending coma occurred, but three days later all the symptoms returned and the patient died. A similar result was obtained in two other cases of diabetic coma, the one complicated by a carbuncle, the other complicated by gangrene of the foot. In neither of these cases was there more than transient effect on the coma.

Transfusion was also performed in a case of diabetes complicated

by pernicious anemia in a young woman.[20] Two transfusions were done in this case, each time with a marked effect on the anemia, but none on the glycosuria or the occurrence of acetone and diacetic acid in the urine. The patient subsequently died of the pernicious anemia, which was of the rapidly progressive type.

Transfusion then had no effect on diabetic coma or on the course of a severe diabetes.

VII. Transfusions for Debilitated Conditions. Now that transfusion has become a relatively easy and perfectly safe procedure, it can be applied to the relief of anemia from all sorts of causes. In cancer there is no reason to expect real benefit from it except in connection with a radical operation. A number of the cases described above under the heading Transfusions Preliminary to Operation, were such cases, and were very successful. In other wasting diseases, such as tuberculosis, transfusion may be indicated to relieve anemia and improve the general resistance of the patient.

There are many cases of simple anemia due to malnutrition or to minor causes or to no assignable cause. In some of these cases ordinary treatment is unsatisfactory or too slow, and transfusion would seem to be justified. In 2 such cases, the one anemic from no definite cause, the other as a result of repeated small losses of blood from hemorrhoids, transfusions were done with most satisfactory result.

Part III.

Notes on the General Management of Transfusions.

1. *Dangers and Complications of Transfusion.* Is transfusion dangerous to the patient? The idea is still widely prevalent that it is; and yet we believe that to-day transfusion has become one of the most certain and safe of procedures. The three classes of accidents that formerly were feared—those due to incompatible blood, to dilatation of the heart, and to introduction of air—are all easily preventable by taking suitable precautions.

Accidents due to incompatibility of blood, that is to say, to hemolysis or agglutination of the red blood cells of either donor or patient by the serum of the other, have been fully discussed in a previous article by Ottenberg and Kaliski.[21] Hemolysis is by far the greater danger and was found both clinically and experimentally[22] to show accurate correspondence between the test-tube phenomenon and the occurrence in the body. *In no case in our series in which hemolysis or agglutination did not occur in the test tube were any untoward symptoms observed which could be attributed to these phenomena.*

[20] We are indebted to Dr. Buerger for permission to use this case.

[21] Loc. cit.

[22] Ottenberg, Kaliski, and Friedman, Jour. Med. Research, 1913, xxviii, 141.

There were 3 cases in which agglutination of the donor's red blood cells by the patient's serum was observed in the test tube. Two of these patients died shortly after transfusion, and in the blood smears of both of them phagocytosis of red blood cells by leukocytes was observed. In the of these cases agglutination was the only test-tube phenomenon, in the other hemolysis as well as agglutination. In the third case the patient's serum was hemolytic to the donor's cells, and an extensive hemoglobinuria occurred after the transfusion, from which, nevertheless, the patient recovered. There was a fourth case, an emergency in which no tests whatever were made (a brother being taken as donor), and in which the patient died with convulsions during the transfusion. The patient, however, was already in bad condition (hemorrhage following nephrotomy for calculus), and it is not certain whether death was due to transfusion or not. It seems probable that it was, however, as the fatal transfusion was the second one in this case, and at the first transfusion much difficulty had occurred in finding a donor because the patient's serum was powerfully hemolytic to the blood cells of most of the donors examined.

The instances in which the donor's serum is agglutinative toward the patient's cells have been shown by one of us[23] to be theoretically far less dangerous; and, in fact, we have seen five transfusions of this kind in none of which were there any untoward symptoms or any phagocytosis in the circulating blood. We have been able to avoid transfusions in which the donor's serum was hemolytic to the patient's cells. In the great majority of cases it is possible by examining five or six different people to find one whose blood is entirely compatible with the patient's. Twice in our experience transfusion has been given up because the patient's serum was found to be powerfully hemolytic to the cells of every donor examined. In one of these instances, however, only a few donors were examined, and it is likely that if a large number could have been examined a suitable donor could have been found.

We feel absolute confidence, then, that if the tests have been carefully done nothing whatever need be feared from this source. It is needless to say that these tests require expert work and a well-equipped laboratory. They take about three hours to perform, and should never be omitted except in the most urgent cases.

The danger due to dilatation of the heart depends not only on the condition of the patient's circulation but on the amount of blood transfused and the rate at which it is delivered. When the patient's heart is known to be embarrassed, transfusion should be interrupted every few minutes. *The amount of blood to be transfused should be decided on before each transfusion* according to the principles we will discuss below. In can be controlled during

[23] Ottenberg, Jour. Exper. Med., 1911, xiii, 425.

a syringe transfusion by direct measurement and during a direct transfusion by the method of calculation which we have introduced.

We have twice seen hypertransfusions. The first case was the rapidly fatal case described above under the heading of Endocarditis. The second case was a case of pernicious anemia in which a large transfusion was performed, the hemoglobin being raised from 15 to 52 per cent. During the transfusion the patient developed all the signs of a pulmonary edema with nausea and vomiting. On the day following there was generalized edema with continued pulmonary edema and hematuria. On the third day the patient developed jaundice. She gradually recovered from these urgent symptoms, but the rapid blood destruction which had been going on continued, and she died three weeks later.

Slight jaundice occurred in 2 other cases. The one was probably an instance of Banti's disease (one of our early cases; incomplete records were kept of the case, so that it was not included in the tabulation of the present series). We believe that the jaundice was probably due to the same cause (excessive transfusion) possibly accentuated by the special hemolytic tendency of the disease itself. In the other case in which a slight jaundice followed transfusion the patient was suffering with a carcinoma of the stomach with numerous metastases.

Hematuria also occurred in 1 other case. It was a case of nephritis with uremia and anasarca. This case was not discussed above under the subject Indications for Transfusions. A phlebotomy of 400 cubic centimeters was followed by a very large vein-to-vein transfusion. It was impossible to follow the amount of blood being transfused by the calculation method because the patient's and donor's hemoglobin were practically the same at the start. Transient hematuria occurred which may have been due to excessive transfusion, but more likely to a special permeability of the kidneys from nephritis, since red cells were found in the urine also at other times independent of the transfusion.

Aside from these unfavorable reactions due to incompatible blood or to hypertransfusion, a more or less marked febrile reaction occurred in about 10 per cent. of all our cases, and skin eruptions, usually urticarial in character, occasionally a few petechiæ, appeared in another 10 per cent. In no instance were these symptoms serious, and in every case they cleared up within three days.

2. *The Donor.* The securing of donors always offers a certain amount of difficulty on account of the necessity of examining a number of men in order to be certain to find someone whose blood is compatible with that of the patient. We have generally inserted an advertisement in the newspapers. Occasionally relatives of the patient have been used, but, as has been shown elsewhere,[24] it is

[24] Ottenberg and Kaliski, loc. cit.

quite as necessary to make the blood tests of relatives as of strangers. In New York there is never any lack of response to advertisements, and we make a practice of keeping a reserve list of men who have answered such advertisements and who can be reached by telephone or otherwise, for use in emergency transfusions. The applicants never object to the taking of about 5 c.c. of blood for hemolysis tests and Wassermann reaction. Sometimes a small stipend is given to them for allowing this to be done.

It is important to know what to tell donors and what can be promised them. They can freely be promised absolute safety and a minimum of pain. When a syringe transfusion is to be done they are able to go to work again the next day. When a direct transfusion is done the wound hampers work for a week or two and in these cases the amount of money paid the donors is usually larger. We have only once known the donor to have any subsequent trouble from transfusion. This was due to an infection of the wound, caused by his own carelessness. In the great majority of instances the recovery of the lost blood by the donor after transfusion is surprisingly rapid, and several donors have been in perfect health and have been used again for transfusion a month or six weeks after the first transfusion. *It is wise in every instance to have the donor before the transfusion sign a legal form, relieving the patient and the surgeon from further liability, and stating the amount of money that he is to receive.*

Aside from the blood test a physical examination should be made to rule out infectious disease (especially tuberculosis and syphilis) or any cardiac condition which would contra-indicate the use of a particular donor. The physical build and temperament of donors are to be taken into consideration. Large men (weighing one hundred and sixty-five pounds or over) are to be preferred, as more blood can be taken from them with safety. Very fat men are not desirable, because in proportion to their weight their blood volume is less. Men of nervous or timid temperament should not be taken, as their actions are likely to interfere with the success of the transfusion. For syringe transfusions the character of the superficial veins is important.

The watching of the donor during transfusion is more important in direct than in syringe transfusions. The donor should be given fluids, such as soup and hot coffee, but whisky should be avoided, as it frequently causes vomiting and does not seem to do any good. The actions of different men during the loss of blood is exceedingly variable, and for this reason the observation of the donor is not a very reliable guide in transfusion. The pulse more frequently becomes slow than rapid. Toward the end of the transfusion it usually becomes soft, sometimes dicrotic. If the pulse rate becomes less than sixty it is best to stop the transfusion. Often the appearance of the patient is unchanged until a sudden collapse occurs.

Sometimes repeated yawning occurs toward the end of the transfusion, as an indication that enough blood has been taken. The first signs of collapse are sweating and pallor, and when these occur a real collapse almost invariably follows, with thready or imperceptible pulse, semiconsciousness, and vomiting. Recovery usually takes place without any special stimulation. We have only once seen a severe collapse that required active steps to be taken. This was a transfusion in a case of shock due to typhoid perforation in which an unusually large transfusion was done, and on account of the patient's desperate condition little attention could be paid to the donor. However, with stimulation the donor recovered in about a half-hour and had no further trouble. In a number of instances large amounts of blood (three pounds or more) are known by actual weighings to have been transfused without causing serious trouble.[25]

If sufficiently long periods are allowed for the hemoglobin percentage to reach the normal again the same donor can be used for repeated transfusions, and there are certain advantages in doing this.

3. *The Technic of Transfusion.* What is the best method of performing transfusion? This is not the proper place to enter into an extended discussion of questions of technic, but since the technic often plays a very important part in determining whether a transfusion should be done or not we will briefly consider the advantages of the several methods. The syringe method, as practised by Lindeman, possesses great advantages over other methods. It involves no trauma and very little pain, and thus does not add the shock of a surgical procedure to the burden of an already sick patient. The exact amount transfused is always known. Not the least advantage is that syringe transfusions can be done repeatedly on the same patient as often as desired. This opens all sorts of new possibilities in transfusion therapy. To some it will appear to be a disadvantage that the syringe method requires a more expensive apparatus. This, however, is no real obstacle. The aspiration of blood from the donor should not be left to an untrained assistant, as this part of the procedure is quite as difficult as the injection into the patient.

The disadvantage of the direct transfusion is that it is a cutting operation and destroys a vein of the patient, so that only a limited number of repeated transfusions can be done. When the patient does not have a low percentage of hemoglobin at the start of the transfusion it also has the disadvantage that one cannot estimate how much blood is being transfused. We believe that those undertaking to do transfusions should be skilled not only in the use of the syringe method, but also in the direct method conducted by means of the Elsberg cannula or Carrel suture. It may be necessary at times to use one of the latter methods.

[25] Libman and Ottenberg, loc. cit.

We have had no experience in the use of anticoagulants, such as hirudin and sodium citrate. In hemorrhagic diseases, which constitute so important a part of the indications for transfusion, such anticoagulants would seem to be contra-indicated. Dr. Richard Lewisohn (personal communication) has made studies of the value of hirudin added to the blood to be transfused and finds it to be not harmless.[26] There are reports that sodium citrate can be used without danger. The method of defibrination is open to the same objection in hemorrhagic conditions as the use of anticoagulants—namely, that it removes fibrinogen and blood platelets. Moreover, it is impossible to defibrinate blood without mechanically injuring the red blood cells to a certain degree, and there is a possibility that if a large amount of defibrinated blood is transfused the antithrombin of the patient's blood will not be sufficient to neutralize the action of the thrombin in the defibrinated blood and that intravascular clotting will occur.

In the great majority of the transfusions reported in the present paper the direct method—artery-to-vein or vein-to-vein—was used. In about twenty of the later transfusions the syringe method was used.

4. *Amount of Blood to be Transfused.* The quantity of blood to be transferred should always be determined beforehand by consideration of the following data:

(*a*) The weight of the donor.
(*b*) The weight of the patient.
(*c*) The condition of the patient.
(*d*) The nature of the disease.

The first two factors have been discussed by us in a previous paper.[27] The third has been considered above under Dangers in Transfusion. As far as the nature of the disease influences transfusion the following conditions may be considered:

1. *Hemorrhage.* In hemorrhage an effort should be made so far as possible to replace the lost blood. Experience, however, shows that collapse can be overcome and the patient brought into a condition of safety by a smaller amount than has been lost.

2. *Hemorrhagic Diseases.* In hemorrhagic disease a relatively small transfusion (500 c.c. for an adult) is usually enough unless the amount of blood already lost has been very large. In hemorrhages due to cholemia we believe that a large transfusion with perhaps a preliminary phlebotomy is indicated (see Cholemia).

3. *Anemias.* When it seems desirable to raise the hemoglobin to a given point it is important to remember that there is generally a rise of the hemoglobin within twenty-four hours to a percentage somewhat higher than that at the end of the transfusion. We have observed this in the majority of our cases in which there was

[26] Dr. Lewisohn believes that various preparations of hirudin vary in toxicity.
[27] Libman and Ottenberg, loc. cit.

no hemorrhage after the transfusion. Generally the rise is about 5 per cent., but sometimes it is as high as 10 per cent. It is presumably due to a concentration of the blood. In pernicious anemia a moderate-sized transfusion (500 c.c. to 1000 c.c.) is probably sufficient.

4. *Poisoning.* In the various forms of poisoning, especially in gas poisoning, a large phlebotomy followed by a very large transfusion would seem to be indicated.

5. *Repetition of Transfusion.* As suggested above, there are probably many conditions in which repeated transfusions will accomplish a great deal more than a single large transfusion, or in which the repetition of transfusions may become necessary at later stages of the disease. Some such conditions are pernicious anemia, hemophilia, and infections, whether local or general. There is no danger in repeated transfusions provided the tests for hemolysis and agglutination are carefully done. The likelihood of hemolysis occurring is distinctly greater in the second and third than in the first transfusions, due to the development of immune hemolysins. We have found this experimentally,[28] and several of the cases of fatal hemolysis after transfusion reported in the literature are instances of second transfusions. In 21 of our cases there were two transfusions, and in 3 of them three transfusions, without any special ill effects.

ADDENDUM. Unger[29] has eliminated the difficulties experienced in the Lindeman method by the use of a simple apparatus. Up to the present time his apparatus has been used in twenty cases. Transfusions can be performed very rapidly, 60 c.c. on an average being transferred per minute. Chills, rises of temperature, vomiting and other symptoms that are occasionally seen after transfusions, seem to be less frequent when this method is used than when either the Lindeman or citrate methods are used. We can regard Unger's method as at present the best for direct transfusion.

Hustin,[30] of Brussels, in May, 1914, published animal experiments in which citrate of soda was used and citrate of soda mixed with glucose. He stated that he had successfully used in one human case a mixture of blood and saline solution containing citrate of soda and glucose. He diluted the blood with an equal amount of saline solution because he feared that the 0.2 per cent. strength citrate which he was using in the blood might be dangerous if the blood was not diluted. This method would limit the size of transfusions and apart from that more recent studies have shown that such dilutions and the use of glucose are not necessary. At a meeting at the New York Academy of Medicine at which the present

[28] Ottenberg, Kaliski, and Friedman, loc. cit.

[29] Jour. Am. Med. Assn., 1915, lxiv, 582.

[30] Ann. et Bull. de la Soc. Royale de Sci. Méd. et Nat. de Bruxelles, 1914, No. 4, p. 104.

writers communicated some of their studies, Weil stated that he had successfully done transfusions in human beings using a 1 per cent. strength of citrate of soda and transferring amounts of blood up to 250 c.c. The coagulation time of the blood of the patients was not prolonged, in fact shortened.[31] Lewisohn[32] has reported the successful use of citrated blood in large amounts using only 0.2 per cent. of the salt. He feared that the percentage of citrate used by Weil would be toxic when large amounts of blood were transfused.

Weil believes that the great value of the citrate method lies in the fact that the blood may be kept on ice for a number of days and repeated injections of small amounts used. He has done 200 transfusions in 46 cases.[33] He usually injected 300 to 350 c.c. of blood, but in one case he used 1400 c.c. The strength of sodium citrate was 1 per cent., occasionally 0.3 per cent. The blood was used as late as six days after it was obtained, but usually within three days. The reactions after transfusion were unimportant. There was occasionally chilliness and headache. In six cases the temperature rose to 102° F. and in four cases, above 102° F. Polyuria occurred frequently. The patients seemed to hold the blood well. The coagulation time was frequently cut in half very shortly after the transfusion, but returned to the original time within twenty-four hours.[34]

Lewisohn has transferred 25 cases; the highest amount given at one time was 900 c.c., but in one case 1600 c.c. were transfused within twenty-four hours. There was a diuresis in most cases which stopped within twenty-four hours. Some patients suffered from headache, and some perspired profusely. He has confirmed all of Weil's observations concerning coagulation time. It is important that he has found that the solution can be sterilized without losing any of its value. In three of his cases a chill resulted and in five there was marked temperature reaction. The chills occurred less frequently, however, than they occurred in Lindeman's series.

We have seen all these newer procedures used and believe that the method of Unger and the citrate method are at present the methods of choice. For large transfusions many will prefer the Unger method. The citrate method has distinct advantages when one wishes to make repeated injections of blood. Apart from its great simplicity it will be of particular value when patients live at a distance or when it is desirable that the patient does not realize that an im-

[31] Weil, Med. Rec., New York, January 23, 1915, lxxxvii, 164; see also Jour. Amer. Med. Assn., January 30, 1915, lxiv, 425.

[32] Med. Rec., New York, January 23, 1915, lxxxvii, 141.

[33] These facts were presented by Dr. Weil in a communication made to the American Society for the Advancement of Clinical Investigation, May 10, 1915.

[34] Dr. Lewisohn's publication will appear shortly in the Journal of Surgery, Gynecology and Obstetrics. We are indebted to both Dr. Weil and Dr. Lewisohn for giving us these facts in advance of their publications.

portant procedure has become necessary. If future studies demonstrate that citrated blood acts as well in pernicious anemia as uncitrated blood and if no disadvantages are found from its repeated use in cases of hemorrhagic disease, this method will prove the most widely applicable.

GASTRIC GLANDS IN MECKEL'S DIVERTICULUM.[1]

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Some time ago the writer performed an autopsy on a child aged nineteen months, who had died as a result of intestinal hemorrhage. There was a history of one previous attack from which it recovered, but had always been rather weak and ill nourished.

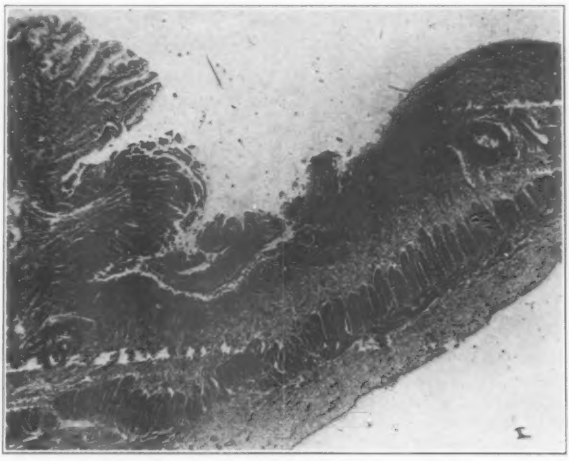

Fig. 1.—Low-power picture showing, from left to right, gastric type glands, villus of ileum, ulcer, and ileal mucosa. The artery at the right is a section of the vessel that ruptured.

At autopsy the skin and mucous membranes were pale, as were all the internal viscera. With the exception of the intestine the latter showed nothing remarkable.

Intestine. About 75 cm. from the cecum on the border of the ileum opposite its mesenteric attachment was a diverticulum, 2 cm. in length and 2.5 cm. in diameter, attached to the posterior wall of the cecum at its apex by a fibrous band 0.4 cm. in width. On section there appears a punched-out, regular ulcer, 0.5 cm. in

[1] Published with the permission of the Surgeon-General, United States Army.

diameter, in the ileum at the border of the diverticulum. In the margin of this ulcer is a small vessel, the lumen of which is plugged with pinkish clot.

The walls of the diverticulum are from 0.4 to 0.6 cm. in thickness, and the mucosa resembles that of the fundus of the stomach. There was no macroscopic blood in the intestine. Death did not occur until thirty-six hours after the hemorrhage, and the movements had ceased to contain blood for twelve hours.

Microscopic examination shows an ulcer extending through the mucosa. The base of the ulcer is made up of a dense layer of fibrous connective tissue infiltrated with polymorphonuclear leukocytes and lymphoid cells. Section taken through the blood-vessel

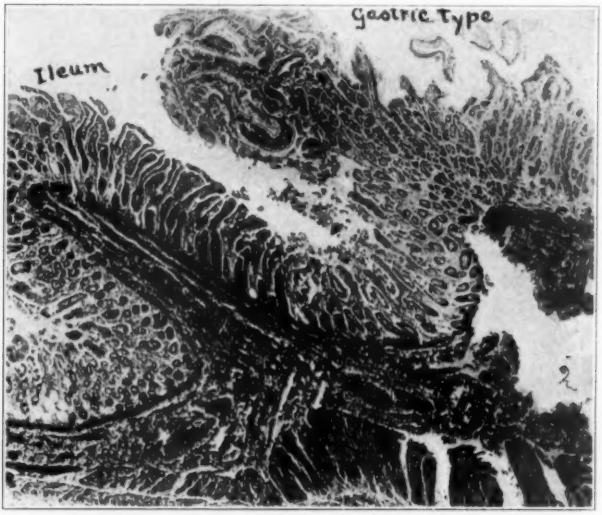

FIG. 2.—Intermediate power, showing junction of mucosa of gastric type with that of the ileum.

shows it to be a small artery filled with a relatively acellular, fibrinous thrombus. A section through the ulcer, and extending into the diverticulum, shows from the border of the ulcer, first a layer of ileal glands, then with a rather sharp demarcation, superficial glands having no goblet cells but epithelium of high columnar type with clear peripheral cytoplasm. This epithelium extends to the bases of crypts into which simple tubular glands empty by narrow mouths. These latter glands form a thick layer extending to the musculosa, and are lined by two types of cells, as in the fundal glands of the stomach. The chief, central, or adelomorphous cells are of low columnar or pyramidal shape, stain rather faintly with eosin, and contain relatively few granules. The parietal, acid,

oxyntic, or delomorphous cells, largely at the peripheries of the glands on the basement membrane, take the eosin stain deeply and are filled with fine granules. The musculosa consists of two layers, an inner circular and an outer longitudinal.

DIAGNOSIS. Peptic ulcer of the ileum; Meckel's diverticulum, lined with mucosa of the type of the gastric fundus glands.

REMARKS. The usual structure of Meckel's diverticulum is that of the ileum: two thin layers of muscle and a mucosa made up of few villi and crypts of Lieberkühn, with occasional areas of

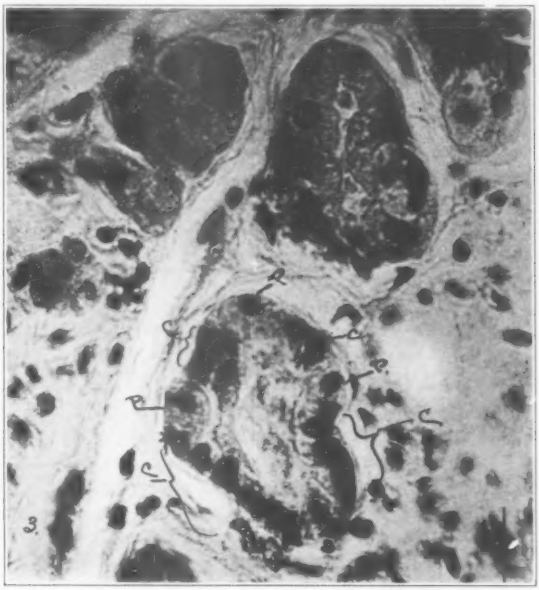

FIG. 3.—High power, showing (*C*) chief and (*P*) parietal cells of the tubular glands. (Stain, eosin-methylene blue.)

lymphoid tissue. They are found about 80 cm. from the ileocecal valve, and are formed by the incomplete closure of the vitelline duct.

A search of the literature revealed no similar case. Hedinger,[2] in 1906, reported a case in which there was an island of pancreatic tissue intermingled with Brunner's glands at the apex of a Meckel's diverticulum.

Acknowledgement is due Doctor C. A. Riley, of Allston, Massachusetts, through whose courtesy the writer was enabled to perform the autopsy.

[2] Corr.-blatt. f. Schwiez. Aerzte, Basel, 1906, xxxvi, 395.

GASTRO-INTESTINAL STUDIES, NO. X: AN ANALYSIS OF ACHYLIA GASTRICA.

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Achylia gastrica stands at the bottom of the long list of secretory disturbances as the expression of the total lack of both enzymes and secretion. Various authors have tried to picture a characteristic clinical syndrome, but the fact remains that the recognition of achylia gastrica can only be made through a direct examination of the intragastric mechanism. This means that an examination of the gastric contents is absolutely essential, although some observers claim that its presence can be recognized by fecal examination. In a summary of the many contributions to this subject, it is evident that the time-worn method of the administration of the test meal and its removal in one hour have been employed. This means that the commonest of all misdiagnosed conditions in this field can scarcely be separated. I refer to the spurious achylias which I shall discuss in the latter part of this article. The introduction of the functional method opens up a new line of study in this field. It enables us to follow the transit of food through the entire cycle of gastric digestion into the duodenum, and there we find a more or less characteristic observation in true achylia, namely, the passage of food into the intestine which is similar in every way to that merely macerated by saliva, for instance, and not chymified. In a true achylia, and speaking broadly I mean a complete achylia, there is no evidence of gastric secretion in any phase of gastric digestion. Not only is there no free hydrochloric acid and practically no total acidity, but pepsin and rennin are lacking. This is rarely the case in gastric neoplasm. Today from the classical studies of Pawlow as well as many other observers we divide the gastric secretion into psychical and chemical phases. The psychical secretion we have been able to demonstrate with normal individuals. If this be true, therefore, that there is a definite psychical secretion initiated through the pathway of the vagus, whose tonus is probably maintained by certain internal secretions (probably parathyroids (?) and possibly thyroids (?)), and a definite chemical secretion incident to the formation and absorption of substances elaborated in the course of digestion, so-called secretagogues and hormones, it should follow that suppression of either of these phases should lead to a psychical or chemical achylia. The investigation of the entire gastric phase would then give us information as to the possible failure of one

or the other of these secretions. A total absence of secretion during the first hour of digestion followed by a perceptible secretion in the second would favor this view-point, namely, that a psychical achylia (nervous) exists, the reverse a pronounced secretion during the psychical phase would favor the interpretation of a chemical achylia. A total lack of secretion through both phases might indicate a deficiency of both functions, or an inactive mucosa, or possibly the failure of material in the blood from which the gastric secretion is derived.

Our studies have indicated that in the majority of cases a complete achylia occupying both phases occurred. We have, however, found several cases in which there was a manifest achylia for one hour or more followed by a perceptible secretion in the second phase, namely, a true nervous or psychical achylia. The reverse, a chemical achylia we have never encountered.

Until we know fully the mechanism and actual formation of the gastric juice, the definite causes producing these secretory phenomena must escape us. It is of interest to note, for instance, that after parathyroidectomy, Carlson and Keating[1] were able to demonstrate a marked deficiency in gastric secretion which was aided and improved by calcium salt administration. On the basis of this observation, in two cases of pronounced persistent achylia of long duration, one of them over ten years, we were able to demonstrate a perceptible and distinct return of secretion during the first hour of digestion. Dr. Bergeim, in our laboratories, elaborated an interesting hypothesis on the origin of gastric hydrochloric acid.[2]

According to this hypothesis the hydrochloric acid is formed from the NaCl of the blood through the interaction of this substance with an acid phosphate in the gastric cells. It was suggested that the acid phosphate was more probably the Ca acid phosphate than acid Na phosphate, because *in vitro* it is much easier to decompose NaCl by the action of the Ca salts. This is due to the fact that the acid Ca phosphate readily hydrolyzes with the formation of a basic Ca phosphate and free phosphoric acid, while the Na salt does not do this. According to him the formation of such an acid salt in the gastric cells presents no great theoretical difficulty, as organic P compounds, particularly nucleic acids, are found in all tissues, and are associated with enzymes capable of splitting off the phosphoric acid. Further, the nucleic acids appear often to exist in combination with Ca. According to this view, the organic P compound may be furnished by the blood. The findings of high acidity and efficient digestion associated with hyperfunction of pituitary and thyroid and the opposite in hypofunction, as well as decrease in secretion after parathyroidectomy, are interpreted to

[1] Keeton, Amer. Jour. Physiol., 1914, xxxiii, 25.
[2] Proc. Soc. Exp. Biol. and Med., 1914, xii, pp. 21-22.

indicate an influence of these glands over the mobilization and decomposition of the organic P compound.

This question is worthy of extended study and investigation, and is mentioned owing to its interest and importance in connection with the cases which we report here.

Discussion of Cases.—The results in these cases are recorded in terms of $\frac{N}{10}$ NaOH, the pepsin was tested by the mett method, and in cases where rennin is marked absent, undiluted content failed to act on milk.

Case I.—Mr. E., patient, was a perfectly healthy young farmer up until a short time before admission into the hospital, when he developed trouble with the ankle-joint and knee-joint on the left side; the patient otherwise was in perfect health, and said that his stomach in no way bothered him. The tube was passed and retained, and specimens removed at fifteen-minute intervals. In one and a half hours after the administration of an Ewald meal the stomach was found to be empty and the rapid motility characteristic of that condition was found to be present. Patient's nutrition was satisfactory and the intestines were able to maintain, to a remarkable degree, their vicarious function.

Time.	Total acidity.	Free acidity.	
15 minutes	1.0	0	
30 "	1.5	0	
45 "	2.5	0	no enzymes
60 "	2.5	0	
90 "	3.0	0	

These figures are practically equivalent to a total absence of all secretion, and the enzymes were lacking. A study of the specimens collectively and separately showed no mucus, no blood, no evidence of any pathological cytology, in fact, nothing but a wet achylia with absolutely no evidence of inflammation. In this case the whole phase shows achylia, and in the absence of any evidence of inflammation, fermentation, bacterial action, and any local or constitutional disturbance incident to the gastric condition, I can only consider the condition a glandular one. Unfortunately, further studies were impossible. Vicarious intestinal function was almost complete.

Case II.—Mrs. B., aged fifty years, four months loss of appetite; loss of weight; pain in the epigastrium, and in fact everything which suggested gastric carcinoma; no palpable mass; no vomiting. This case, which is of great interest, was in the service of Dr. Solis Cohen, in the Jefferson Hospital, and it was with his kind permission and coöperation that I was enabled to study the case. Owing to the lack of appetite and the epigastric pain, the patient had refrained from eating and lost considerable weight.

Examination revealed a soft, rather relaxed abdomen, in which the stomach could be distinctly outlined by inflation extending

to the level of the umbilicus, absolutely free from any palpable masses, and in which no tender points could be palpated; nor was there any splash or clapottage. The passage of the fractional tube on the empty stomach failed to reveal any appreciable residuum, and there was no retention or food rests, and no hypersecretion. An Ewald meal was then given, and after the first few samples, which were rather liquid, material having all the characteristics of a dry achylia was removed. The material was removed at intervals until the one and three quarter-hour interval, when the

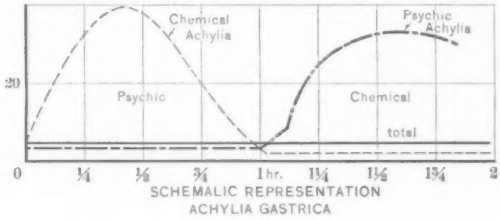

FIG. 1

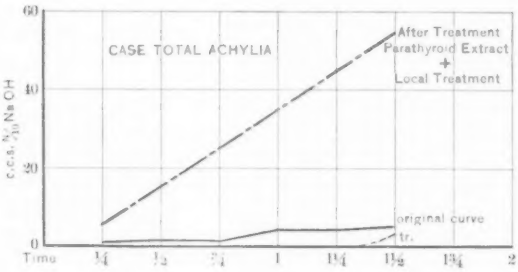

FIG. 2

stomach was found to be empty—a lavage confirmed this finding. The results of this first examination are as follows:

Time.	Total acidity.	Free acid.
20 mins.	1.0	0
30 "	3.0	0
40 "	2.5	0
1 hour	1.0	0
1¼ hours	4.0	0
1½ "	4.0	0
1¾ "	low	0

This was repeated three days later with the same findings.

An examination of different portions revealed neither pepsin

nor rennin, nor was there mucus, occult blood, or bacteria in any of the specimens. The albumin reaction did not exceed $\frac{1}{80}$ in any phase, and there were no cytological findings, no lactic acid was found, and absolutely no signs of putrefaction. I was compelled, on the strength of this examination, to make a diagnosis of benign achylia, and shortly after Roentgen-ray examination revealed absolutely nothing in the stomach. Examination at that time revealed a small palpable mass in the inner aspect of the cecum corresponding to the appendix, and toward this were peristaltic waves, small intestinal, indicating a probable obstruction in this region. An achylia diet was instituted; the patient was given parathyroid extract, and shortly afterward commenced to gain weight. In a comparatively short times her appetite had returned.

A second test several weeks after the first observation revealed the following curve:

Time.	Total acidity.	Free acid.
5 mins.	7.0	0
15 "	15.5	Trace
30 "	11.0	Trace
45 "	3.0	0
1 hour	8.0	0
1½ hours	....	0

Shortly afterward she continued to improve, and in the interval gained seven pounds, was free from pain, and eating liberally. Her subsequent history was not so satisfactory; shortly afterward she suffered from grippe and was readmitted into the hospital in very bad shape; marked headache; severe pain in the back; lassitude; and a mass in the right side; 23,000 leukocytes; probable carcinoma of cecum, with infection and abscess formation. Her condition was so poor as to prohibit intervention, and she died, without permission from the family for an autopsy. Of one thing I am certain, that in this case the gastric sumptoms were not due to carcinoma ventriculi. The mass in the right side was small and insignificant, and was probably an early carcinoma of the cecum. In this case all the improvement, as shown in two examinations, was on the psychical side of the curve—no improvement was noticeable later in the curve—and the case is of interest as registering a distinct improvement under parathyroid.

Case III.—The following case was a very intelligent gentleman, M. P., referred to me by Dr. Nylin. To all intents and purposes he was perfectly healthy, and there were no gastric symptoms whatsoever. He complained only of looseness of the bowels, from which he had suffered for many years; it was scarcely looseness, rather than an undue frequency of the bowels. Careful examination showed high blood-pressure 160, accentuated aortic, very early signs of interstitial changes in the kidneys, some gouty tendency. Examination of the movement showed a malassimilation of car-

bohydrates and connective tissue in small amounts. His curve was as follows:

Time.	Total acidity.	Free acid.	Pepsin.	Rennin.
15 mins.	3.1	0	0	0
30 "	3.1	0	0	0
45 "	3.0	0	0	0
1 hour	6.0	0	0	+
1¼ hours	4.0	0	+ trace	++
1½ "	23.0	Trace	0.5[2]	++
1¾ "	31.0	Trace		

This case is extremely instructive. It shows according to the ordinary technique, an achylia, but by the fractional method it shows a total psychic achylia, distinct evidence of a chemical

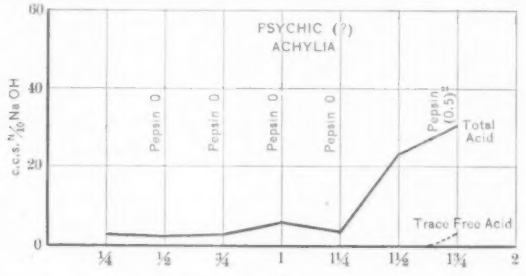

FIG. 3

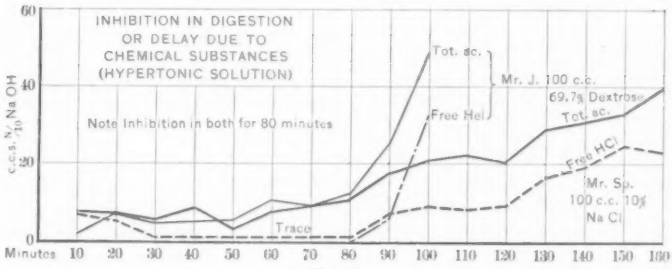

FIG. 4

secretion during the second phase. This has been endured for years, and yet there was absolutely no evidence of any irritation on the part of the stomach, no bacteria, mucus, or blood—simply a dry achylia, from which juice was filtered, with difficulty in the first phase and distinctly more abundant in the second phase. Furthermore, evidence of both pepsin and rennin were found throughout later phases.

CASE IV.—Mr. K. was referred by Dr. Beardsley and Dr. Tracey, Beverly, New Jersey. This case was one of unusual interest, inasmuch as it presents the many phases and causes which might be

operative in causing an organic achylia and in which a bad prognosis was fortunately incorrect. Mr. K., aged forty-seven years, hard worker, and exposed to considerable nervous tension, has been suffering for many years from an obscure gastric condition. Ten years ago, when seen by Dr. Musser, he was found to have an achylia with gastric catarrh and dilatation. At the time when I first saw him his condition was deplorable, his appearance a grayish green, and markedly anemic. He complained of bringing up a small amount of yellowish mucus every morning. His condition to the attending physicians suggested a pernicious anemia, and I must confess that it seemed that such a course was likely, although a complete blood picture and certain signs were atypical. Wassermann was negative, and before I made a gastric study, another physician had made an examination, found a great deal of pus and mucus in the stomach, and a complete achylia according to the ordinary methods. The empty stomach revealed little retention, but a great deal of mucus, and the fractional examination after the administration of the Ewald meal showed the following:

Time.	Total acidity.	Free acid.	Mett pepsin.	Rennin.
5 mins.	1.0	0	0	0
15 "	1.0	0	0	
30 "	1.5	0	0	
45 "	1.5	0	0	0
1 hour	4.0	0	0	
1¼ hours	4.0	0	0	
1½ "	5.0	0	0	0

Total achylia in every phase, an enormous amount of mucus, pus which had been clearly swallowed, many bacteria, some swallowed and others intimately mixed with the contents; *no enzymes;* absolutely no response, and tinged throughout in each case with blood. Neoplasm ruled out, owing to the duration, the relatively low loss in weight, absence of mass, and of any Roentgen-ray findings and the diagnosis of achlorhydria hemorrhagica gastrica secondary to ingestion of infected mucus from probable bronchiectosis in lung. To make a long story short, diet was immediately regulated, lavage and the direct local application of silver was carried out, iron and arsenic given hypodermically, and parathyroid given, gr. $\frac{1}{10}$, t.i.d., for three days at intervals. After three months he had gained twelve pounds in weight, his blood had gone up to 4,200,000, his hemoglobin over 80 per cent., his appetite had completely returned, but the important thing was the gastric analysis, after an achylia of ten years' duration, in which we all felt justified in believing there was an atrophic gastritis:

Time.	Total acidity.	Free acid.	
15 mins.	6.0	0	
30 "	....	0	
45 "	15.0	0	
1 hour	35.5	Trace	Pepsin present.
1½ hours	55.0	Strong trace	Free acidity.

Rennin—not tested.

Still some mucus, but infinitely less than on former occasions, and a few bacteria which have been gradually stamped out. I am not prepared to believe that the parathyroid is entirely responsible for this change. In fact, the hypodermic administration of hematinics may have wrought a change; furthermore, I acted on the principle that nutrition was the important thing in his case, increased assimilation being followed by marked improvement. Among the interesting points in this case was the return in the salivary secretion to which the patient himself called attention; furthermore, the tongue, which was glossy and rather pale at first, became bright red, with papilla distinct. The bowels, which were markedly constipated, phenomena of mucus colitis being frequent, were once more regulated, although it must be confessed a small amount of magnesia was and is being used. It is my belief that parathyroid is in part responsible for the return of the secretion, inasmuch as qualitative tests on other occasions did not reveal such a pronounced effect. The gain in weight was from 131 to 158 pounds, and at this writing, nine months later, the cure is complete.

Case V.—Represents Mrs. Si., aged thirty-eight years, who has been suffering for three years with nausea and vomiting and an obscure gastric affection which suggested neoplasm. Her curve shows an absolute achylia in every phase and no enzymes. Abderhalden reaction was negative, and Roentgen-ray studies show, outside of marked ptosis of both stomach and large bowel, no evidence of any neoplastic condition. Stool examinations show connective tissue which has come through, but otherwise poor utilization of fats. The case exhibits also hyperthyroidism, and is at present under observation. There is undoubtedly a marked catarrhal process present, and two examinations at an interval of two weeks reveal complete achylia:

Time.	Total acidity.	Free acid.	Pepsin.	Albumen.	Rennin.
5 mins.	2.0	0.0	0	..	0
10 "	2.5	0.0	0	80	0
15 "	3.0	0.0	0	..	—
30 "	4.0	0.0	0	..	—
45 "	4.45	0.0	0	..	—
1 hour	6.0	0.0	0	80	0
1¼ hours	5.0	0.0	0	..	—
1½ "	10.0	Trace	0	80	? 30 min.
1¾ "	9.0	?	0		

Gastric mucus in every specimen.

Digestion of an Ewald meal is over in one and three quarter hours. It will be seen that there is practically no elaboration of acid; there is, however, a trace to be found in the more advanced stage of digestion. There is a large amount of mucus, illustrative of a pronounced catarrh. The question which arises is naturally that between a neoplasm, a benign achylia, and a pronounced infected gastritis (achlorhydria hemorrhagica gastrica). Against the former is the

blood count, the condition of the patient, the peculiar type of the albumin curve, which in that condition steadily increases. Furthermore, there is to be found no lactic acid, no Oppler-Boas bacilli, but some small diplobacilli and bacteria.

CASE VI.—Contrast the preceding with the following case of spurious or false achylia in a case of marked gastric catarrh.

Mrs. H., suffered from typical loose bowels—with apparently no definite cause, indigestion, discomfort, eructations after eating. Occasionally cramp-like pain in the upper abdomen. Empty stomach negative, except for small residuum almost entirely composed of gastric mucus.

An Ewald meal gave on fractional examination the following results:

Time.	Total acidity.	Free acid.		
5 mins.	2.0	0	Mucous	
10 "	2.0	0	Mucous	
15 "	3.5	0	—	
30 "	4.0	0	—	
45 "	4.0	0	—	—pepsin +
1 hour	5.0	0	—	—pepsin +
1¼ hours	3.5	0		
1½ "	15.5	0	—	—pepsin +
1¾ "	23.6	0		Rennin—not tested.

Here was a case of chronic gastritis with hypermotility and the typical gastrogenous diarrhea incident to a lack of gastric secretion. Undoubtedly the case would be placed in the achylia group, and yet pepsin, when properly activated, was found when tested. There is here once more a complete inhibition or delay of the psychical secretion to be followed by an appreciable secretion during the second stage of gastric digestion. The specimens in this case answered the description of wet achylia. After thorough irrigation and treatment of the stomach, perceptible free acid was found earlier in the digestive cycle.

(NOTE.—At present writing, some six months later, well; but incomplete return of secretion.)

CASE VII.—Mrs. Gr. is a case in every way similar to the case described as Case VI. Empty stomach is negative, but in this young woman, who complains of discomfort and distress after eating, no actual pain shows the following findings after the administration of an Ewald meal:

Time.	Total acidity.	Free acid.	Pepsin.
5 mins.	4.0	0	0
10 "	4.0	0	0
15 "	5.0	0	0
30 "	7.0	Trace mucus	+
45 "	11.0	Trace mucus	+
1 hour	29.0	6.0 mucus	+
1¼ hours	30.0	Trace mucus	++
1½ "	6.0	mucus	
1¾ "			

Prolongation of digestion; still an appreciable rest after two hours; intimate mucus in all the specimens, indicating a well-marked catarrh; occult blood negative; starch digestion advanced; yeast, trace; lactic acid, slight trace; many bacteria indicating an infected mucosa; likewise vegetable debris, but no meat, there being atony and stagnation.

Spurious achylia, catarrh, atony, dilatation (?)

We have been able to demonstrate an experimentally induced achylia even in hypersecretory individuals by means of certain hypertonic solutions. The results of this work will appear shortly but it seems proper to state that both hypertonic salt solution and dextrose solutions are capable of inducing a definite delay in the appearance of gastric secretion for eighty minutes or more. This is of considerable interest inasmuch as water alone is capable in these subjects of giving rise to a perceptible secretion.

In conclusion we may state:

1. True achylia in which there is a total lack of acid and enzymes through the entire period of gastric digestion is exceedingly rare.

2. By means of the fractional method we have been able to study the entire period of gastric digestion in cases of achylia. On the basis of Pawlow's work, it is suggested that if his conception of gastric secretion be correct, it should follow that achylia can be either psychical or chemical. A total absence of secretion in the first hour of digestion, followed by a perceptible secretion in the second, would favor the belief that a psychical achylia (nervous) exists. The reverse, falling off in secretion, would favor the interpretation of a chemical achylia. A total lack of secretion through both phases might indicate a deficiency of both functions or an inactive mucosa.

3. Our studies show that the commonest form is a complete lack of gastric secretion through both phases (total achylia); two cases were encountered of true psychical achylia, but a pure chemical achylia was never encountered.

4. Attention is called to spurious achylia, which is quite common, and in which there is an ultimate elaboration of juice late in digestion, and always enzymes present.

5. By means of the administration of parathyroid extract in two cases of *bona fide* achylia, one of over ten years' duration, a perceptible return of the gastric secretion was noted during the psychical phase. Dietetic and local treatment were instituted at the same time.

6. The phase method of examination is of great value in determining the type of achylia as well as the possibility that at some phase the secretion might still be active, as shown in several of the cases recorded. This finding distinctly improves the prognosis.

ALTERNATION OF THE PULSE: A COMMON CLINICAL CONDITION.

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The purpose of the present communication is, in the first place, to express the frequency of pulsus alternans as a clinical condition, and, secondly, to report the analysis of histories, clinical findings, and cardiographic records of this series of cases. I have found alternation of the radial pulse in 71 patients in the wards and among the out-patients of the Massachusetts General Hospital during a period of eight months. Radial pulse tracings were taken from 300 cardiac and cardiorenal cases in all.

Pulsus alternans is that condition of the pulse in which strong and weak beats alternate, but in which the cardiac rhythm is normal. It includes constant alternation and alternation found in phases and after premature beats only. The pseudo-alternation due to the late appearance of premature beats and due to respiratory influences must be differentiated from the true alternation (Figs. 2, 3, 6, 7, 8, and 9).

The clinical literature on the subject includes reports of small numbers of cases, usually from one to four or five, with scarcely a hint that all around us alternation of the pulse lies undiscovered. Mackenzie[1] has seen the condition often during a considerable number of years, and now has records of "over 100 cases," collected during a decade or more. Windle,[2] in 1913, reported 45 cases collected during a period of over four years.

Gravier,[3] in 1914, published a thesis in which, at considerable length, he discusses the theories of alternation and the experimental work on the subject, and details a study of 40 cases which he had collected with the help of Gallavardin during the course of two years. I would refer to his extensive bibliography for the literature on the subject.

Neither Mackenzie, Windle, nor Gravier[4] express the frequency of alternation of the pulse. They indicate that it is not rare. It is the writer's aim to show that it is a common condition.

In the present communication the alternation found in the rapid pulses of auricular flutter (Figs. 1, 2, and 3) and paroxysmal

[1] Diseases of the Heart, 1913, p. 260.

[2] Quart. Jour. Med., 1913, vi, 453.

[3] L'Alternance du Cœur, Etude Critique et Clinique, Paris, 1914.

[4] Gravier makes a prophecy on page 270 of his monograph "L'Alternance du Coeur" as follows: "Il ne fait donc pas de doute pour nous que le pouls alternant ne soit bientôt reconnu comme un *symptôme frèquent* de l'insuffisance cardiaque."

tachycardia (Fig. 4) is not included.[5] Also, the pseudo-alternation due to respiratory blood-pressure changes (Figs. 5, 6, and 7) and to delayed appearance of premature beats (Fig. 8) is excluded. Doubtful cases of true alternans have been omitted. Of the 71

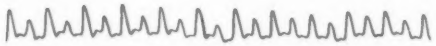

FIG. 1.—Pulsus alternans in a patient about two hours after the onset of an attack of auricular flutter. In tracings one hour and one and one-half hours after the onset of the flutter at the same rate as the present (144) no alternation occurred. Time interval = 0.2 second.

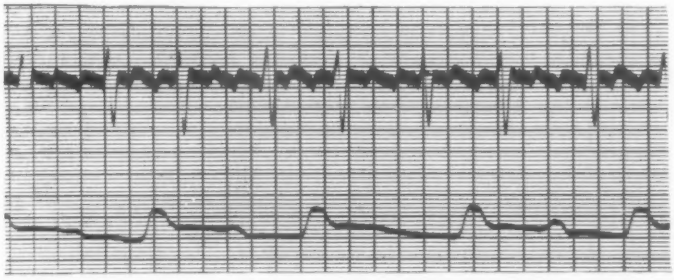

FIG. 2.—Pseudo-alternation from a case of auricular flutter. Simultaneous records of Lead II of the electrocardiogram above and radial pulse below. Abscissæ = 0.2 second. Ordinates = 10^{-4} volts.

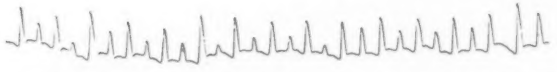

FIG. 3.—Radial tracing from patient whose record is shown in Fig. 2. Pseudo-alternation of auricular flutter. Time interval = 0.2 second.

cases found, 15 showed a constant alternation, 55 a post-premature beat alternation only, and 1 a phasic alternation.

[5] During the eight months, three patients showing flutter and one showing paroxysmal tachycardia had alternation, the latter displaying the condition only at a rate of 185 and not at the lower paroxysmal rates of 150 and 100, or at the normal rate of 60, a fact which reveals the exhaustion rate of this heart.

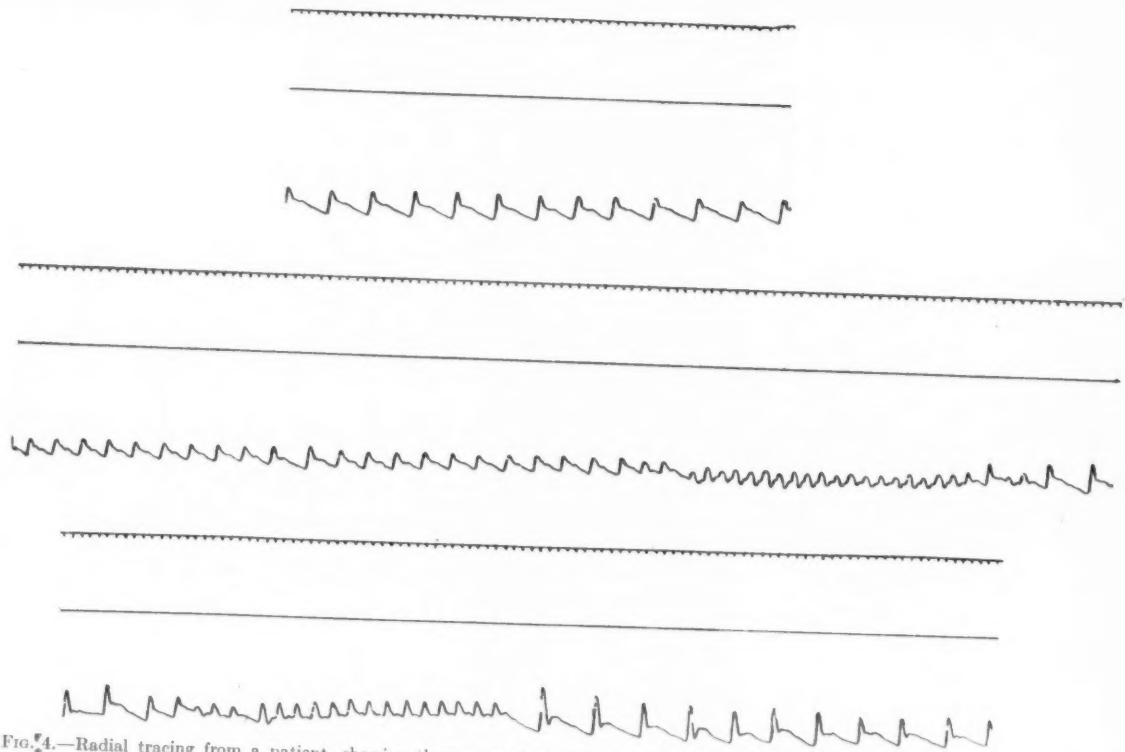

FIG. 4.—Radial tracing from a patient, showing three rates of paroxysmal tachycardia. Interval of a few seconds between strips of tracing. Upper tracing shows the normal rate (60); middle tracing shows two rates of tachycardia (first 100, second 185); lower tracing shows a short paroxysm at a rate of 150, with return to the normal rate of 60. Alternation is present in the pulse at the highest rate only. Time interval = 0.2 second.

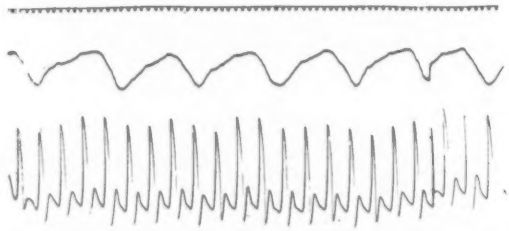

FIG. 5.—Simultaneous respiratory and radial tracings, showing well the respiratory change in the force of the pulse. In this instance pulsus paradoxus is present. In the respiratory record the rise of the curve represents expiration and the descent inspiration. Respiratory rate is 25, pulse rate 92 per minute. Time interval = 0.2 second.

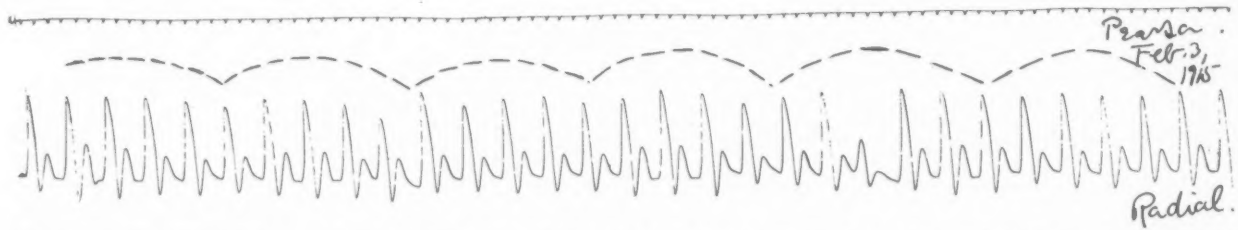

FIG. 6.—Pseudo-alternation following first premature beat. No alternation after second premature beat. Line of dashes represents the respiratory changes in the pulse volume. The first premature beat is followed by a natural rise in the volume while the second premature beat is followed by a drop. Hence the alternating beat after the first premature beat is due to respiratory and not myocardial conditions. Time interval = 0.2 second.

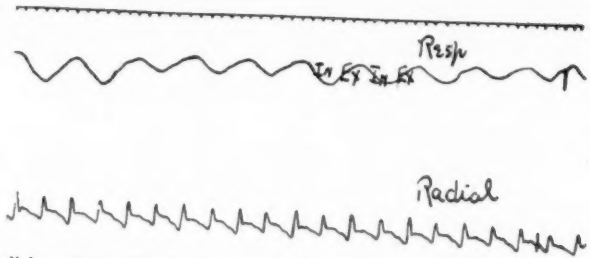

FIG. 7.—Simultaneous respiratory and radial tracings. Respiratory rate is 55 and pulse rate 110 to the minute. The alternation is due here to this exact relationship, and is not a true alternation. Downstroke in respiratory curve represents inspiration, upstroke expiration. Time interval = 0.2 second.

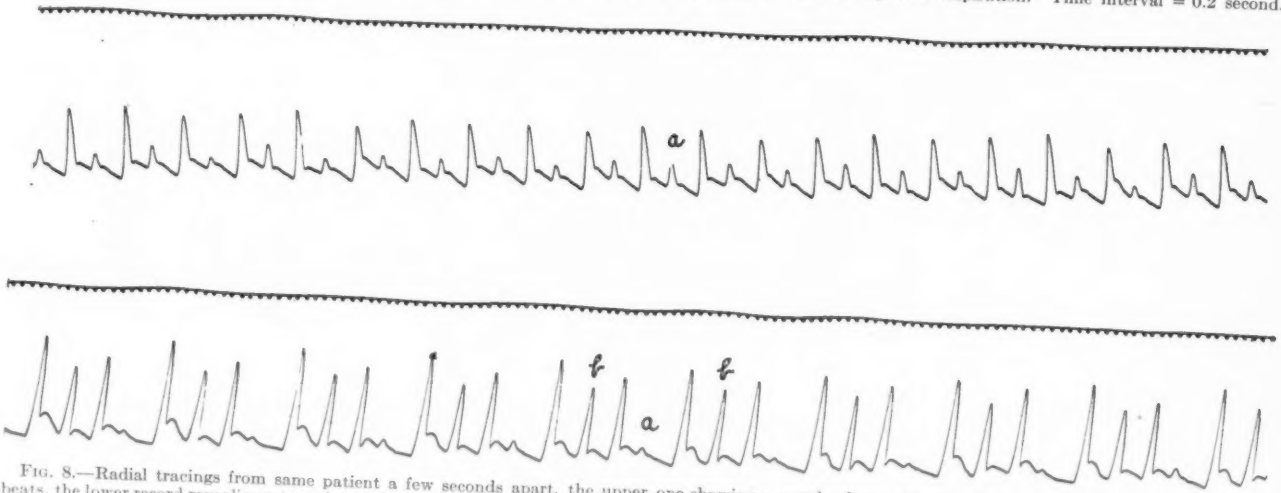

FIG. 8.—Radial tracings from same patient a few seconds apart, the upper one showing a pseudo-alternation due to bigeminy from ventricular premature beats, the lower record revealing a true alternation following a ventricular premature beat which falls every fourth beat. *a* = ventricular premature beat. *f* = weak alternating beat. Time interval = 0.2 second.

The findings by months has been quite uniform, 8 to 10 being the usual figure. From August 1, 1914, to November 30, 1914 inclusive 33 cases were found, and from December 1, 1914, to March 31, 1915 inclusive 38 more were discovered, making a total of 71 for the eight months. On the two medical services of 40 to 50 beds each, 51 patients were found to have pulsus alternans, 18 out-patients showed the condition, and 2 cases were found in the surgical wards. The medical services received the closest observation, although in these undoubtedly a few cases slipped by unrecognized and untraced. Among the out-patients and in the surgical wards relatively little time was spent. During two recent months in the out-patient department of the hospital, Dr. J. H. Pratt and four medical students limited their attention entirely to cardiac cases, and found among them 6 cases of alternation (8 per cent. of 74 from whom radial tracings were taken).[6] This fact indicates that during eight months in which I studied the condition, probably less than half of the out-patient alternations were missed.

The frequency of alternation as compared with other abnormalities of the heart beat found by me at the Massachusetts General Hospital in eight months may best be shown in tabular form:

TABLE I.

Ventricular premature beats	119 cases
Pulsus alternans	71 "
Auricular fibrillation	71 "
Auricular premature beats	22 "
Defective *A–V* conduction and block, including twelve bundle branch lesions (long *As–Vs* interval not preceded by digitalis administration)	21 "
Paroxysmal tachycardia	9 "
Auricular flutter	6 "

Alternation of the pulse was found in 33 per cent. of all cases showing any degree of cardiac decompensation from whom a radial pulse tracing was obtained. Table II shows the relative frequency of the various abnormalities of the heart beat in decompensation.

TABLE II.

Cases of cardiac decompensation traced in eight months	201
Pulsus alternans	66 (33 per cent.)
Auricular fibrillation	65 (32 per cent.)
Normal pulse	24 (12 per cent.)
Ventricular premature beats without alternation	20 (10 per cent.)
Defective conduction without alternation following digitalis	12
Defective condition with and without alternation following digitalis	19
Defective conduction without alternation not following digitalis	8
Defective conduction with and without alternation not following digitalis	20
Auricular premature beats without alternation	4
Auricular premature beats with and without alternation	8
Auricular flutter	2

[6] The writer is indebted to Dr. Pratt for these figures.

Seventy-two cases of non-fibrillating hearts showing hypertension (systolic blood-pressure constantly above 160 mm. of mercury) were examined, and of these 37, or *51 per cent.*, showed alternation. The association of alternation and hypertension has been pointed out by Windle,[7] Gravier,[8] Lewis,[9] and others, and among the cases reported in the literature, hypertension occurred in a large percentage.

The relationship of age to pulsus alternans in the 71 cases is shown in Table III.

TABLE III.

Years of age.	Number of cases of pulsus alternans.	
0 to 10	0	11 (15 per cent.) below the age of forty.
10 to 20	2	
20 to 30	2	
30 to 40	7	
40 to 50	16	44 (62 per cent.) above the age of fifty.
50 to 60	17	
60 to 70	17	
Over 70	10	

The youngest patient was fifteen years of age[10] and the oldest seventy-five years. The majority of Windle's patients were old arteriosclerotic people.

SEX. Of the writer's series 49 (69 per cent.) were male and 22 (31 per cent.) female.

In the attempt to determine the etiological factors of the cardiac condition the following data have been obtained:

TABLE IV.

Clear history of rheumatism, chorea, or tonsillitis	9 cases	(13 per cent.)
Clear history of syphilis	4 "	(6 per cent.)
Wassermann test positive (of 60 cases tested)	9 "	(15 per cent.)
Hypertension: systolic pressure constantly above 200 mm. mercury	12 "	(17 per cent.)
total constantly above 160 mm. mercury	37 "	(52 per cent.)
diastolic pressure (of 68 cases tested) above 100 mm. mercury	32 "	(47 per cent.)
Age, patients over fifty years[11]	44 "	(62 per cent.)
Excessive alcohol	13 "	
Excessive tobacco	12 "	
Excessive tea or coffee	11 "	

[7] Loc. cit. [8] Loc. cit. [9] Clinical Disorders of the Heart Beat, 1914, p. 104.

[10] A few days after the expiration of the eight months a girl, aged ten years, was discovered to have true alternation of the pulse.

[11] The relationship of the arteriosclerosis of old age and pulsus alternans has been studied by tracing the radial pulse of 69 patients at the Massachusetts State Hospital at Tewksbury and at the Long Island Hospital, City of Boston. Among these arteriosclerotic people, nearly all over sixty years of age, but few presented much evidence of cardiac decompensation, 5 showed alternation of the pulse, 4 in but slight degree after premature beats, 16 showed auricular fibrillation, 14 ventricular premature beats, 5 auricular premature beats, and 2 defective *A–V* conduction. The oldest patient, aged ninety-seven years, showed ventricular premature beats but no pulsus alternans; she looked as though she might readily live to be ten years older in spite of her marked peripheral arteriosclerosis. I am indebted to the resident physicians of the hospitals at Tewksbury and Long Island for the opportunity to examine their patients.

The severe acute infections are probably infrequently attended by alternation of the pulse. Of 10 severe cases of pneumonia and 4 of typhoid only 1 (typhoid fever with defective heart) showed alternation.

Digitalis played no part whatsoever in the etiology of alternation in more than half of the cases, for 40 patients had received none so far as I was able to determine prior to the pulse tracing. The failure to find alternation in the pulse of two typhoid patients who had a considerable degree of heart-block from digitalis or in that of two surgical cases in whom a postoperative digitalis blocking was produced (in one of these a prolonged *a–c* interval was found with a pulse rate of 105), suggest that digitalis may have played no role in the causation of the alternation in the other 31 cases of the series.

The relationship of clinical conditions such as angina pectoris to alternation has also been of interest. The present large series of cases affords useful data.

TABLE V.—CLINICAL CONDITIONS ASSOCIATED WITH THE ALTERNATION OF THE PULSE.

Dyspnea (constant or on slight to moderate exertion)	66	cases	(93 per cent.)
Dyspnea without physical signs of decompensation	28	"	(39 per cent.)
Dyspnea with very marked physical signs of decompensation	9	"	(13 per cent.)
Angina pectoris	6	"	(8 per cent.)
Cheyne-Stokes breathing	6	"	(8 per cent.)
Albuminuric retinitis (18 fundi examined)	8	"	
Albuminuria	45	"	
Glycosuria	3	"	
Valve lesions—Mitral stenosis alone	3	"	Total, 15 cases 21 per cent.
Aortic valve lesion alone	4	"	
Aortic and mitral	5	"	
Mitral regurgitation alone	3	"	

Hypertrophy of the heart was usually found on physical examination and 24 cases which were examined with the Roentgen-ray (the patient's chest seven feet from the tube) showed definite cardiac enlargement in every instance. The great vessels were abnormally wide in 5 of the 24 cases.

FINDINGS BY GRAPHIC METHODS.—The pulse of each case was examined with the Mackenzie ink polygraph and 44 of the 71 cases were also electrocardiographed. The following two tables show the analyses of the records made.

TABLE VI.—POLYGRAPHIC RECORDS.

Constant alteration (Fig. 9)	15 cases	(21 per cent.)
Alternation after premature beats only	55 "	(77.5 per cent.)
Alternation after premature beats only (marked) (Fig. 10)	15 "	(21 per cent.)
Alternation after premature beats only (slight) (Fig. 11)	40 "	(56.5 per cent.)
Phasic alternation	1 case	
Ventricular premature beats	67 cases	(94 per cent.)
Auricular premature beats (3 with v.p.bs.)	4 "	(6 per cent.
No premature beats	3 "	(4 per cent.)
Defective A–V conduction (two after digitalis)	3 "	
Paroxysmal tachycardia at other times	2 "	
Pulse rate at time of alternation:		
Under 100 per minute	53 "	(75 per cent.)
Lowest rate, 57; highest rate, 125.		

TABLE VII.—ELECTROCARDIOGRAPHIC RECORDS (44 OF THE 71 CASES WERE ELECTROCARDIOGRAPHED).

Evidence of lesion of right branch of A–V bundle	7 cases	(16 per cent.)
Evidence of lesion of left branch of A–V bundle	0 "	
Evidence of defective A–V conduction (long P–R interval) not after administration of digitalis	5 "	(11 per cent.)
Other cases with long P–R interval after administration of digitalis	7 "	
Aberrant ventricular complexes (other than bundle branch lesion)	3 "	
Total of cases evidencing damage to conducting system (including one discovered with the polygraph)	15 "	(34 per cent.)
Left ventricular preponderance	22 "	
Right ventricular preponderance	3 "	

The T deflection was flat or inverted in 13 and low in 2 of 24 cases who had not been taking digitalis.

Eighteen of the 44 electrocardiograms showed premature beats, and in 7 of these cases there was slight alternation of the T deflections afterward (Figs. 12 and 13), in 6 in accord with the radial alternation and in one in reverse order. In 3 cases there was slight alternation of the R–S deflections after premature beats. No constant alternation of the R–S or T deflections occurred. There was no alternation of the P complexes found.

Sinus arrhythmia was a frequent finding.

TABLE VIII.—SINUS ARRHYTHMIA ASSOCIATED WITH ALTERNATION OF THE PULSE.

Marked	6 cases	(8 per cent.)
Moderate	20 "	(28 per cent.)
Slight	16 "	(23 per cent.)
None	20 "	(28 per cent.)
Questionable	9 "	(13 per cent.)

The small percentage of marked sinus arrhythmia occurring with the alternation is probably accounted for by the relatively old age of the majority of the patients, but the frequency with which some degree of sinus arrhythmia occurred with pulsus alternans in the

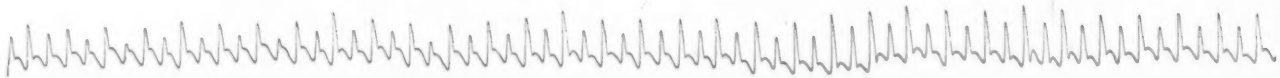

FIG. 9.—Constant pulsus alternans. Rate 102 per minute. Time interval = 0.2 second.

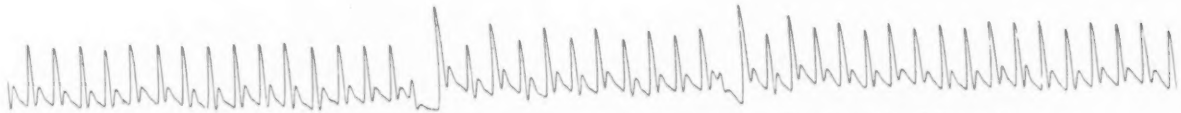

FIG. 10.—Marked postpremature beat alternation. Rate 84 per minute. Time interval = 0.2 second.

FIG. 11.—Slight post-premature beat alternation. Rate 87 per minute. Time interval = 0.2 second.

present series is a noteworthy fact. The response of the heart to nervous impulses may be active, although the cardiac contracting power is much diminished.

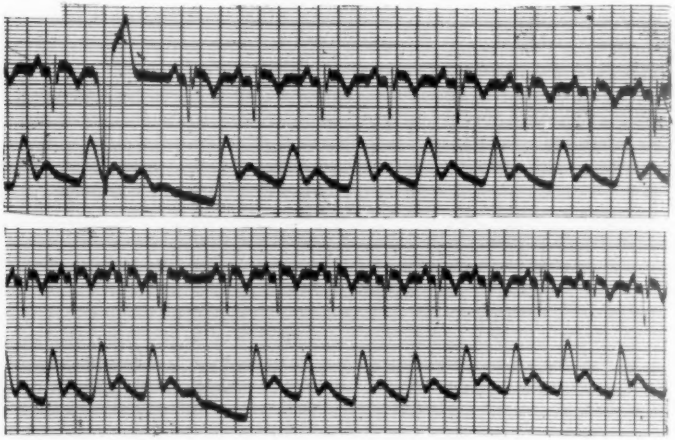

FIG. 12.—Simultaneous records of electrocardiographic Lead II and radial pulse of patient, showing slight post-premature beat alternation. Note slight alternation of the *T* deflections after the premature beats. Time interval = 0.2 second.

THERAPY. Digitalis was given to 53 of the 71 cases and clinical improvement followed in 32 cases (60 per cent.), illustrating well

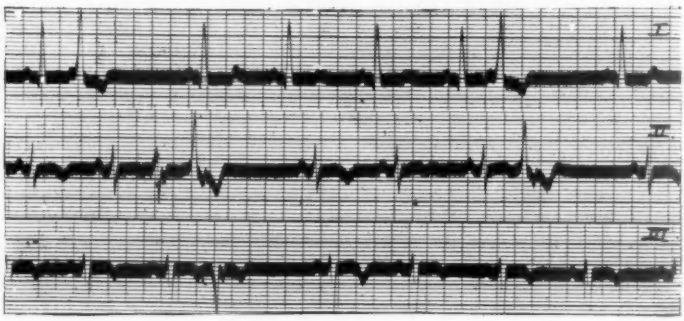

FIG. 13.—Leads I, II, and III of patient who showed slight alternation of the radial pulse after ventricular premature beats. Note post-premature beat alternation of the *T* deflections. Left ventricular preponderance is shown by Leads I and III. Abscissæ represent fifths of a second, ordinates represent 10^{-4} volts.

the fallacy of the old-time belief that it is unwise to give digitalis to an alternating heart. In 4 cases the degree of alternation was

lessened after digitalis, in others judgment could not be passed because premature beats which had appeared and had been followed by alternation no longer occurred after the administration of digitalis.

Prognosis. One of the most important relationships of alternation is that to prognosis. Since but a very short interval has elapsed since the eight months during which the cases here recorded were collected, it is impossible to give more than a suggestion as to the prognostic significance of the pulsus alternans. Twenty-two of the cases (31 per cent.) are known to have died during the eight months, most of them a few months after the condition was discovered. During the ninth and tenth months three more are known to have died, making a total to date (June 1, 1915) of 25 deaths (35 per cent.). Of the 25, one patient is known to have had pneumonia at the time of death, another streptococcus septicemia, a third malignant disease of the liver, and a fourth was comatose following a cerebral hemorrhage. Two of the 25 were below the age of forty years (the younger being fifteen years old) and 13 were over fifty years old; 10 had visited the out-patient department of the hospital within a few months or a few weeks before death; that is, they were ambulatory patients at the time their alternation was in progress.

The relationship of the degree of alternation to prognosis is shown in the following table:

Table IX.

	Number.	Dead.	Percentage.
Cases showing constant alternation	15	8	53
Cases showing marked post p. b. alternation . .	15	7	47
Cases showing slight post p. b. alternation . .	40	10	25

Tabora[12] has spoken of a case of pulsus alternans alive six years after the condition was found; this is the longest survival on record.

Pathological Findings. Of 6 cases dying at the Massachusetts General Hospital, 3 came to autopsy. All 3 showed coronary sclerosis in some degree, and 2 also showed on gross examination of the endocardium areas of fibrosis; 1 case showed marked sclerosis of the aorta.

The weights of the three hearts were high—384 grams, 403 grams, and 475 grams respectively.

Microscopic examination of the kidneys showed in all an arteriosclerotic nephritis.

Value of Methods of Determining Alternation. A graphic record of the pulse is the only satisfactory method in searching for alternation, and even then one must be prepared to take a record of considerable length. This can be done well with an ink sphygmograph, long rolls of paper being available at very little expense and effort.

[12] Conversation with Gravier, "L'Alternance du Coeur," p. 282.

Palpation of the radial pulse revealed the alternation in 13 of the 15 cases showing the condition constantly. It was also felt in several of the cases of post-premature beat alternation, but this finding is very unreliable, because of the impossibility to detect the difference by the finger between very late premature beats (as in a bigeminal pulse) and weak alternating beats. This criticism applies also to Gravier's delicate bimanual method. Rarely this difficulty may also be experienced in the radial tracing itself on measurement. In such instances a simultaneous jugular tracing or, better still, an electrocardiogram will settle the matter.

Auscultation of the heart is notoriously unreliable. Kahn[13] has published experimental phonocardiograms showing the alternation in intensity of the heart sounds in dogs whose hearts were alternating; but when one listens to the hearts of patients whose radial pulse alternates, the difference in intensity of the sounds is slight at the most. In one case of the 71 recorded here who showed very marked constant pulsus alternans, the heart sounds varied not at all in intensity.

Rehberg's test,[14] which consists of the finding of a difference in the blood-pressure of alternating beats is cumbersome but reliable if a graphic record is taken; the auscultatory method in the use of the blood-pressure cuff is unsafe on account of the inaccuracy of auditory measurement in distinguishing between late premature beats and alternation.

Delay in the Appearance of the Small Alternating Beat at the Wrist. This delay was pointed out in the first description of pulsus alternans by Traube[15] himself in 1872, and has been frequently found since. Of the 15 constant alternations in the present series, 6 showed well this delay, 5 showed it slightly, and 4 failed to show any measurable delay. An analysis of 25 post-premature beat alternations shows a simple delay of the small beat or beats in 12 without apparent shortening of the *As–Vs* interval after the premature beat. In 5 cases the *As–Vs* interval after the premature beat was shortened, and in 7 cases there was a combination of this shortening with the usual alternation delay, thus magnifying the delay of the first weak alternating beat (Fig. 14). Sinus arrhythmia sometimes confused the picture slightly, but the curves were studied which showed none or very little.

Other Observations. The relationship of the prematurity of the forced beats to the degree of alternation is seen, as a rule, only in comparison of early beats with those coming so late that they occur almost at the normal point after the preceding beat (Fig. 15). In such cases the alternation is greater after the more premature beat, a condition that would be expected on account of the

[13] Arch. f. d. ges. Physiol., 1911, cxl, 471.
[14] Ztschr. f. klin. Med., Berlin, 1909, lxviii, 247.
[15] Berl. klin. Wchnschr., 1872, ix.

FIG. 14.—Polygram from patient exhibiting slight post-premature beat alternation. The upper record is of the jugular pulse, the lower of the radial pulse. Two auricular premature beats are shown. The *a–c* interval following each premature beat is shortened. Time interval = 0.2 second.

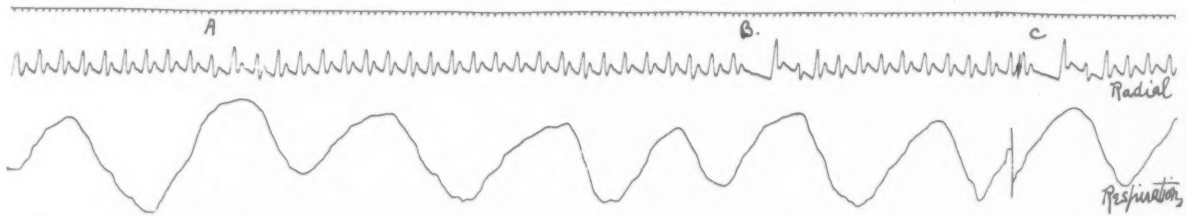

FIG. 15.—Simultaneous respiratory and radial tracings from a patient exhibiting post-premature beat alternation. In the respiratory curve the rise represents expiration and the descent inspiration. The late premature beat at *A* is followed by much less alternation than the early premature beats at *B* and *C*. Time interval = 0.2 second.

greater burden on the heart with the early beat. The alternation preceding premature beats as described by Windle[16] has been seen by the writer only in a patient who, while showing waves of increase and decrease of a constant alternation, happened to have a premature beat soon after the increase had begun. The sixth radial upstroke in Fig. 7 of Windle's paper may represent a late premature beat, thus explaining the alternation following.[17]

The relation of respiration and degree of post-premature beat alternation has been found to consist of a slight increase during inspiration and a slight decrease during expiration with ordinary breathing; with the pulsus paradoxus of thoracic respiration the reverse might be expected.

SUMMARY. True alternation of the radial pulse has been found in 71 of 300 cardiac and cardiorenal patients examined with the sphygmograph by the writer at the Massachusetts General Hospital in the course of eight months (August 1, 1914, to April 1, 1915).

It has occurred as commonly as auricular fibrillation;[18] 66 of 201 cases examined who were suffering from cardiac decompensation in some degree showed pulsus alternans; 65 others of the 201 showed auricular fibrillation; 15 of the patients having alternation showed it constantly, 55 after premature beats only and 1 showed a phasic type. The finding of ventricular premature beats has been of considerable value in the present series, 77 per cent. of the cases requiring the premature beats before the alternation of the pulse was exposed.

The condition was found most often in people in late middle life or in old age. Hypertension was associated with the alternation in 52 per cent. of the cases. Cardiac enlargement was practically a constant finding. Syphilis and rheumatism apparently played a less important part in the production of the myocardial weakness than did arteriosclerosis.

Electrocardiographic examination of 44 of the cases gave evidence of damage to the *A–V* conducting system in 15 cases, or 34 per cent. Electrocardiographic alternation was found in the *T* deflections after premature beats in 7 of 18 cases which showed premature beats on the records obtained. Only in 3 cases was there any alternation of the *R–S* deflection after premature beats.

Sinus arrhythmia occurred frequently in the series.

Digitalis and rest in bed produced clinical improvement in 32 of 53 cases in which digitalis was administered even though the pulsus alternans may have persisted. In 4 cases the alternation was diminished or banished after this therapy.

[16] Heart, 1910, ii, 95.

[17] Gravier has made this same observation concerning Windle's tracing, "L'Alternance du Coeur," p. 151.

[18] In 1906 A. Hoffman (Münch. med. Wchnschr., 1906, liii), wrote of finding 10 cases of complete arrhythmia and 10 cases of alternation of the pulse out of 183 cases traced.

Twenty-five of the 71 cases died within ten months from the beginning of this study, the majority of the deaths so far as could be determined attributable to the cardiac condition directly. The relationship of the degree of alternation to prognosis was as one would anticipate, the greater the degree the shorter the life after the pulse discovery.

Arteriosclerosis of heart and kidneys was found in the only three cases examined postmortem.

It gives the writer pleasure to acknowledge his indebtedness to members of the hospital staff for their coöperation.

MODE OF ACTION AND USE OF EMETIN IN ENTAMEBIASIS.

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The value of emetin in amebic dysentery is so well established that the further report of cases successfully treated would scarcely be of general interest at the present time. The literature on the subject is rapidly becoming voluminous, but the present status of the drug in the treatment of amebiasis has been excellently summed up in a rather recent paper by Vedder.[1] During the past eight months still further facts have come to light, so that the present communication will be limited to a practical discussion of the advances made in our knowledge concerning the mode of action of the drug, best methods of administration, dosage, ill effects, relapses, and other points of interest. In considering the mode of action of emetin in entamebiasis it will be necessary to inquire somewhat briefly into the habits and habitat of amebas in the body, and while some of the views expressed may be later proved incorrect, they at least permit of a rational basis for therapy.

Mode of Action of Emetin and Ipecac in Entamebiasis. The exact manner of action of ipecac and emetin in amebic disease was until a few years ago very indefinite. In the old days of ipecac therapy there were many theories but few facts. It can be stated now from experimental and clinical evidence that emetin is the active principle of ipecac from the amebecidal point of view. In 1912 Rogers[2] by the subcutaneous and intravenous use of emetin demonstrated that it owes its action chiefly at least to absorption

[1] Origin and Present Status of the Emetin Treatment of Amebic Dysentery, Jour. Amer. Med. Assoc., 1914, lxii, 501.

[2] Rapid Cure of Amebic Dysentery and Hepatitis by Hypodermic Injections of Soluble Salts of Emetin, British Med. Jour., June 22, 1912, p. 1424.

into the blood stream with resultant destruction of the amebas in the tissues. It matters not whether the amebas be in the tissues of the colon, liver, or gums of the mouth.

The question arises, Has emetin or ipecac any effect upon amebas not in the tissues or within reach of the circulation but in the lumen of the large intestines? Carter[3] believes that in giving the whole drug (ipecac in salol-coated pills) by mouth and emetin by needle that by the former method we insure that the intestinal contents are thoroughly permeated with the drug and in the latter we reinforce the amebecidal effect of the parent drug upon the parasites buried in the wall of the affected intestines by the hypodermic injections of emetin carried to them by the blood stream. He is convinced that acute amebic dysentery requires the entire root with all its alkaloids as well as emetin. If we accept these statements as true, undoubtedly our new treatment with emetin injections must be modified or rather complicated by the simultaneous oral use of large doses of ipecac. In short, we must return to the old, cumbersome ipecac therapy plus our emetin by needle. Do the facts justify the assertion that by giving ipecac orally we can thoroughly permeate the intestinal contents with the drug? In order to answer this question satisfactorily it is essential to know how ipecac or its active principles are eliminated from the body. Unfortunately all the text-books on modern pharmacology to which I have had access are uniformly silent upon this point. In hope of throwing a little light upon this subject the following investigation was made in 1912.[4] Stools from patients receiving ipecac in which no amebas had been found for at least two or three days were collected, filtered, and the filtrate sterilized by heat. The sterile fecal filtrates were added to growths of amebas *in vitro* and allowed to remain in contact for varying lengths of time. The result was that the amebas remained practically unaffected, showing that the feces contained none at least of the amebecidal constituents of the ipecac. This is the only experimental evidence I am aware of against the elimination by the large bowel of the amebicidal principles of ipecac (chiefly emetin). The experiment, however, still lacks confirmation. Furthermore, it has been demonstrated *in vitro* that emetin (also ipecac) is highly destructive to practically all species of amebas. Even clinically, evidence[5] has recently come to light showing the specificity of emetin on a species of amebas found in the alveolar tissues in Rigg's disease.

There exists in the intestines of many normal individuals the harmless *Entameba coli*. This organism should be easily destroyed

[3] Emetin and Ipecacuanha: Their Amebecidal Value in Pathogenic Amebiasis, Indian Med. Gaz., March, 1914.

[4] Observations on the Effect of Ipecac, Phenol, and Salicylic Acid in Vitro, New Orleans Med. and Surg. Jour., 1912, lxiv, 884.

[5] Protozoa of the Mouth in Relation to Pyorrhea Alveolaris, Dental Cosmos, 1914, lvi, 948.

by emetin (or ipecac) if the drug is eliminated by way of the intestines. The following case will prove of interest in this connection:

In 1913 I had occasion to treat a physician of this city for a chronic diarrhea. He had contracted amebic dysentery in Cuba seven years previously. Two years later he took a thorough course of ipecac, but a moderate diarrhea still continued. In 1912 a sigmoidoscopic examination revealed nothing abnormal. When seen by me in November, 1913, he was having a few loose stools early in the morning, but later the passages would become solid. The stools showed fermentation and were not dysenteric in character. Microscopically there was no blood or pus but some mucus, trichomonads, and also what appeared to me to be typical *Entambœ coli*. Because of the patient's suspicious past history he was given therapeutic test with emetin. One grain of the hydrochlorid was injected daily for seven days. At the end of this period there was no improvement. Examination of the stool still showed vegetative entamebas (small, granular, sluggishly motile amebas, with well-defined nuclei). Under diet, rest, and attention to kidneys the patient was markedly improved.

The result of this case adds further weight to the contention that emetin is not eliminated from the blood stream by way of the alimentary tract otherwise the *Entamebœ coli*, which are simply harbored in the intestines should have been readily destroyed. The non-pathogenicity of the colon entameba is due in all probability to the fact that it does not penetrate the intestinal mucosa. This explains why neither ipecac nor emetin, orally or by needle, has any effect upon them. By analogy the pathogenic entamebas which are free in the intestinal canal should remain unaffected by our specific medication and cause no symptoms. Such is found to be the case in the carrier state. Finally, the amebicidal action of ipecac and emetin is limited then to the amebas in the tissues. When these are all destroyed the lesions heal with remarkable rapidity and the patient is cured.

Relapses and Carriers. Unfortunately in a certain proportion of cases we find that relapses occur or the patient remains well, but his stools still contain the pathogenic entamebas and the individual becomes a carrier. Just why a relapse occurs in one case and the carrier state in another cannot be explained satisfactorily at present. Naturally both conditions depend upon the survival of some of the entamebas.

To enter into a slightly more detailed discussion of this subject might appear, at first sight, to be only of theoretical interest, but it will be found, when we come to therapy, to be of considerable practical value, as we do not treat the two conditions alike.

Relapses, in most instances, are due to the fact that some of the amebas escape destruction by encystment. In this stage they are resistive to any form of medication and produce little, or at times,

no local irritation. From careful history taking in some 80 cases of amebic dysentery I have found that in the majority of instances it will be noted that even in periods of improvement or apparent well-being the patient will usually admit that he experiences some slight abdominal discomfort or unnatural feeling in spite of the fact that the stools were apparently normal. From this I am strongly inclined to believe that in the majority of cases some of the cysts remain imbedded in the tissues of the colon and are not simply harbored in the large intestine in the same manner as the *Entamebæ coli*. For if such were the case there should be complete absence of symptoms in the intervals of remission. The relapse takes place then when conditions are favorable for the encysted forms to again become vegetative.

In the carrier state it would appear however, that conditions are somewhat different. Here the individual who is a menace[6] to the community is himself apparently immune to the organism which simply lives in his intestines. What it is that protects the intestinal mucosa in such a case from penetration by the parasite is not known, but this fact constitutes the essential difference between the two states.

MODES OF ADMINISTRATION. There are at the present time four routes by which emetin has been introduced into the body: the subcutaneous, the intravenous, the oral, and the rectal. It is important for effective therapy to know the advantages and disadvantages of each method. In the following discussion the hydrochloride of emetin will only be considered, with occasional reference to ipecac.

The Subcutaneous and Intravenous Routes. For practical purposes these two methods of administration may be considered together. The intravenous route is only necessary in exceptional cases and does not differ from other intravenous medication.

With regard to the subcutaneous injections of the drug there are several facts to be borne in mind: (1) that the alkaloid emetin is slightly irritating, and (2) the hydrochloride is slightly acid in reaction (the degree of acidity varies somewhat in preparations from different pharmaceutical houses). Where a small dose is injected, such as one-third grain, both of these factors are negligible, as the product is rapidly absorbed into the circulation. On the other hand if a large dose is administered (as one grain) considerable local pain and inflammation results, owing to the concentration of the factors just mentioned. Intramuscular injections cause still more discomfort. The inflammatory reaction thus produced at the site of inoculation may persist as an infiltrated area for from one to two weeks. It is more than probable that such a reaction seriously retards the rapid absorption of the drug.

[6] Walker and Sellards, Experimental Entamebic Dysentery, Philip. Jour. Sci., 1913, Sec. B., No. 4, 253.

For these reasons where prompt and lasting effect is desired, small repeated injections are far preferable to large single doses.

Oral Route. When emetin is administered by mouth it is highly probable, from what has been previously stated, that the drug is absorbed into the blood stream in the small intestines and is not eliminated by way of the colon in the fecal matter. The drug is usually taken in salol or keratin-coated pills:

My first experience with this method occurred in April, 1913, in a man aged forty-four years, with a severe dysentery and hepatitis. Because of the urgency of the symptoms (fever, abdominal pain, large tender liver, and leukocytosis) it seemed important to get the patient rapidly under the influence of the drug. He was accordingly given one-third grain of emetin hydrochloride by needle and by mouth, twice a day, that is, a total of one and one-third grains daily. The emetin was put up in one-third grain salol-coated pills. Ignorant of the contents of the pills the patient thought from the effect that he was taking a drastic purgative. There was considerable abdominal discomfort and a marked increase in the number of stools. After two days it was necessary to stop the drug by mouth and improvement rapidly ensued.

This irritant action of emetin when taken by mouth is well exemplified in a case I was called in to see by Dr. Matas through whose courtesy I am reporting it. The circumstances are briefly as follows:

The patient was a white male, Italian, aged seventy years. Admitted to the Charity Hospital in November, 1913. The disease began one month previous to admission with a bloody diarrhea. The diagnosis of hepatic abscess was made and the patient was operated upon by Dr. Matas. Two days after the operation the patient was put on emetin, and given one grain by needle daily. In less than two weeks he was entirely free from temperature. The patient then refused further injections of emetin because of the soreness of his arms. Thereupon it was decided to continue the emetin by mouth in the same dosage, the ampoules being simply emptied into water. This solution caused no vomiting but his stools began to increase in number. Ten days later, when I was asked to see him, his bowels were extremely loose and he was very emaciated and feeble. Examination of the stools failed to show amebas but there were blood clots, pus, and mucus present. Recalling my first experience with the oral method I advised simply discontinuing the emetin. The patient made a slow but uneventful recovery. When seen two months later he had had no further return of his amebic affection.

Here we have the curious spectacle of a man being cured and killed by the same drug. Undoubtedly the administration of emetin was prolonged unnecessarily. Another surprising fact was the ability of the patient to retain large doses (one grain) of the drug by mouth.

In order to determine the amount of gastric and intestinal irritation produced by the oral ingestion of smaller doses, the writer took a half-grain of the same preparation of emetin in solution. This caused nausea and vomiting after an interval of an hour. This was followed in another hour by two loose stools accompanied by griping, and some abdominal discomfort persisted for five or six hours. After this experience, in order to avoid the psychic element, I gave one-half grain by mouth to an unsuspecting, healthy young negro. He suffered no nausea, but one hour and a half later he had two watery passages with considerable abdominal discomfort.

Low[7] reports good results in two cases of amebic dysentery in which he used keratin-coated tabloids in one-half grain doses at night. Vedder[8] has treated one case by this method without obtaining the striking results that follow the hypodermic use of emetin, and is therefore not in favor of it.

There is sufficient evidence at the present time to state that emetin should be given by mouth only under circumstances that do not permit of the hypodermic methods or of the administration of the whole drug (ipecac) by mouth, and then only in small doses (one-sixth to one-third grain).

Colonic Route. With reference to this method, Chauffard[9] reports a case of amebic dysentery in which under subcutaneous injections of emetin the stools decreased from fifteen to two or three daily. After reading the report of Marchoux on the treatment of dysentery with emetin enemata, he decided to irrigate his patient with an emetin solution (100 mg. to 1000 c.c.). That day the patient had fifteen dysenteric stools. He looked upon this intestinal intolerance as due to the fact that this patient had been previously treated by subcutaneous injections of the drug.

Although I have never used emetin by enema, I am strongly inclined to agree with Vedder that this so-called intestinal intolerance was due to the direct irritant action of the drug on the intestinal mucosa.

The practical value of solutions of either emetin or ipecac for colonic irrigations is problematical, for the vegetative amebas will be easily destroyed if reached by many of our well-known agents, such as quinin, salicylic acid, silver nitrate, and others, while those in the tissues will not be acted upon.

Dosage and Duration of Treatment. The dosage of emetin originally recommended by Rogers was small. The average subcutaneous dose was one-third grain, and a total of two grains

[7] Administration of Emetin by Mouth in Amebic Dysentery, British Med. Jour., 1913, No. 1, 1369.

[8] Loc. cit.

[9] Resultats inattendus d'un Lavement d'emetine chez un Dysenterique Amebien, etc., Soc. Méd. des Hôp., June 20, 1913.

usually sufficed for an apparent cure. Later the pendulum swung in the opposite direction and amounts varying from two and one-half to four grains daily were injected subcutaneously, and even by vein in severe cases. The cause of this reaction was probably due to the fact that as time elapsed reports of relapses became more frequent. At the present time the most effective dose appears to be somewhere between these two extremes. For an ordinary case of amebic dysentery in an adult an average of one grain daily is sufficient. It is of course impossible to dogmatize upon this subject, as individualization is necessary. Mild cases may get along well on less than one grain and severe cases may require more. I have yet to see, however, a case that required more than two grains daily, provided the principle of repeated small injections was followed. The tendency in the early days of the emetin treatment was to stop the injections when the stools became formed. Experience has shown that it is better practice to continue the injections, as Dopter advises, for four or five days after the stools are apparently normal. Careful and systematic examination of the stools will be found to be one of the best guides to therapy.

In general the duration of treatment is from one to two weeks. It is seldom wise to prolong the administration of the drug beyond two weeks even though a diarrheal condition exists unless active entamebas are still present. The diarrheal condition may be due to an intestinal catarrh or an association bacillary infection, or possibly to the drug itself. In two cases that I have recently treated the diarrhea could apparently be attributed to the subcutaneous injections of emetin.

The first case was a college professor of forty years. He was treated by a colleague and put on ascending doses of emetin beginning with one-third grain and increased in four days to two grains a day. During the first few days of the treatment the patient's bowels were checked and the pain and tenesmus subsided. When the large doses of the drug were reached (fourth day) his bowels became loose again and abdominal discomfort returned. When I saw the patient he had taken a total of nine grains of emetin. As no amebas could be found the dose of the drug was reduced for a few days and then discontinued. The patient returned to his home and after two or three weeks the bowel disturbance disappeared. There has been no recurrence in the past four months.

The second case was a young colored male of twenty-eight years who had had a chronic dysentery for five or six years. He was given injections of emetin (one grain) daily for twelve days. Like the former case he at first improved rapidly, then an obstinate diarrhea set in. Examination of the stool showed blood-tinged mucus and a few resting amebas. The emetin was stopped and a saline enema given daily for five days, during which time the number of stools was notably lessened. Following this a short

course of emetin by needle was again instituted. At the end of this course the stools were normal and a sigmoidoscopic examination negative.

These two cases favor the view that too large doses of emetin or too prolonged use of moderate doses may cause a diarrhea or be responsible for its persistence. In what way the subcutaneous injection of the drug causes intestinal irritation I am unable to explain. At all events, emetin is best administered in courses of a week to ten days and repeated at intervals if necessary. During the administration of emetin, moderate purgation with castor oil or a saline is often beneficial. It keeps the intestinal tract clean and mechanically washes out many of the entamebas in the gut. For a number of years I have made it a rule not to discharge a patient until he has been given a large dose of salts (one ounce), and the effect on the bowels carefully noted. In some cases that were thought to be cured, dysenteric symptoms returned and active amebas were found in the stools. The salts may be said to act as a therapeutic check upon our cures, though too much reliance should not be placed upon it.

Ill Effects of Emetin. Ill effects from emetin are rarely encountered unless the dosage is large or the administration prolonged for too long a time. I have already mentioned the probability of emetin by needle producing or keeping up a diarrhea. Allen[10] has produced nausea and vomiting by a single dose of four grains; no other ill-effects were noted. A mild peripheral neuritis occurred in a physician under my care who took, while in the country, one and one-third grains of emetin daily for sixteen days. During the last few days of the injections his legs became weak and he suffered with pains especially in the calves. There was also some general muscular weakness. This condition gradually cleared up after stopping the drug. Eshleman[11] reports a case that developed a general eruption, purpuric in character, associated with a severe peripheral neuritis. The patient had received two grains daily for five or six days. Weis[12] has observed peripheral neuritis in two cases following emetin, and believes it to be due to the use of too large doses. Spehl and Colard[13] report a case that had been given one grain for six days and then the dose increased to one and one-half grains daily. After a few days the patient developed a flaccid paresis of all muscles. There was edema of the face, rapid pulse, and diminished tendon reflexes. Recovery was slow. Serious symptoms have been met with after the intravenous[14] use of large

[10] The Emetin Treatment of Amebic Dysentery, Jour. Amer. Med. Assoc., 1913, lx, 664.

[11] Bull. of Touro Infirmary, New Orleans and Surg. Jour., 1914, lxvi, 965.

[12] Ibid.

[13] A Case of Emetin Poisoning, Provence Medical, April 18, 1914, p. 176.

[14] Baermann and Heinemann, Die Behandlung der Amoeben Dysenterie mit Emetine, Münch. med. Woch., 1913, lx, 1132.

doses of emetin. It will be found safer to adhere to the original dose proposed by Rogers for intravenous use (one grain).

In experiments on animals Vedder and Nichols[15] have demonstrated that the drug is fatal to certain laboratory animals in comparatively small doses (2.5 mg. per kg. of emetin intravenously, fatal to rabbit). The evidence is increasing in the literature to the effect that the drug is not as harmless as generally supposed and that large doses are not without danger.

Relapses and Carriers. As mentioned in a previous paper[16] it is not always easy to state, in many instances, whether a relapse is a reinfection from within or a fresh infection from without. In reviewing my own cases and the literature in general I should judge approximately 25 per cent. of the cases have recurrences. Under ipecac therapy relapses appeared to be less frequent, though I doubt seriously if this were actually the case. It is quite true that patients once treated with large doses of ipecac[17] rarely return for a second course, at least, to the same physician, for many of them prefer to suffer the inconvenience of the disease or try a patent medicine. On the other hand few individuals object to the emetin treatment and readily return if not cured. Willets[18] believes that the apparent superiority of ipecac in percentages of cures is due to the fact that the dosage of emetin varied widely as well as its mode of administration, while the ipecac cases were treated more persistently than the emetin cases. Siebert,[19] who has had a wide experience with ipecac, considers the effect of emetin more lasting and that fewer cases relapse in the same time with emetin than with ipecac.

The pathology of relapse has already been discussed, and we find that they are due probably to the fact that some of the amebas in the tissues escape destruction by encystment. Attention to the principles of administration, dosage, and duration of treatment previously outlined will prevent relapses in some instances. Where the stools still contain entamebic cysts after apparent cure a recurrence is likely to occur. As these cysts cannot always be found it is a safe rule where possible to place all patients on the intermittent plan of treatment. I have followed, in a general way, Chauffard's[20] method, which consists in giving a second series of injections two weeks after the first, then a third after three weeks, and even a

[15] Loc. cit.

[16] Lyons, R., Treatment of Amebic Dysentery with Subcutaneous Injections of Emetin Hydrochloride, Jour. Amer. Med. Assoc., 1913, lx, 1216.

[17] Exception should be made in favor of aleresta ipecac which is not disagreeable to take.

[18] Preliminary Report on Treatment of Entamebiasis with Ipecac, Emetin-Neosalvarsan, Philip. Jour. Sci., 1913, ix, 93.

[19] Ueber die Behandlung der Amoeben ruhr mit Emetine, Archiv. f. Schiffs und Tropen-Hygiene, 1914, xviii, 439.

[20] Les Rechutes de la Dysenterie Amibienne et leur Traitment, Jour. des Prat., 1914, xxviii, 38 to 40.

fourth after a like interval. In long-standing cases this may be continued at monthly intervals. The drug is given for four or five successive days. The dosage that I have used has been usually one-third grain, morning and evening. Before instituting the treatment the patient is given one ounce of salts in the morning and the first injection administered after the bowels have acted several times. This method was adopted in the hope that the intestinal congestion and watery stools caused by the saline might produce conditions favorable for the encysted entamebas to again become vegetative, when they would readily be affected by the emetin injections. There is no proof to this effect except, as previously stated, that intestinal irritation favors recurrences.

It is too early to predict what the ultimate effect of such plans of treatment will be on the percentages of relapses, as prolonged observation will be necessary. The principle, however, is rational and the number of relapses should be markedly diminished. From our knowledge of the pathology of the disease and the habits of the organisms it was scarcely to be hoped that one course of emetin or any other drug would be curative in every case.

In the treatment of carriers, emetin has not achieved much success. Local irrigations of the bowel are usually resorted to, though emetin is too irritating for this purpose. Fluidextract of ipecac may be substituted. Vedder advises high irrigation with quinin or silver nitrate solution. As it is a question of destroying resistant entamebic cysts, persistent and systematic treatment is required.

Emetin in Pyorrhea Alveolaris. The treatment of Rigg's disease with emetin originated from the discovery of Smith and Barrett[21] that amebas were present in the gums of individuals afflicted with the disease. These investigators injected a 0.5 per cent. solution of emetin hydrochloride into the pyorrheal pockets which resulted in marked improvement of the condition. Bass and Johns[22] after an extensive investigation of over 200 cases of Rigg's disease confirmed the observations of Smith and Barrett and concluded that the disease was caused by a specific ameba (*Entamba buccalis*), which could be found in practically every case. They further improved the treatment by the subcutaneous use of the drug, injecting (in any part of the body) usually one-half grain of emetin daily for three to six days. They do not consider local injections of the drug into the gums necessary in every case, but do advise the use of a drop or two of fluidextract of ipecac on the tooth-brush at night. This will prevent further infection or relapses and may also be employed as a prophylactic measure.

[21] Loc. cit.

[22] Further observations on pyorrhea alveolaris, Bass and Johns, New Orleans Med. and Surg. Jour., Feb., 1915, lxvii, 671.

Four cases were recently reported by the writer[23] in which the disease was apparently cured by the subcutaneous use of emetin. It is too early to consider the question of relapse in this disease or to state whether further injections or courses of emetin will be needed to maintain a cure. The tendency of amebas to encyst and the fact that emetin by needle only affects amebas in the tissues must be borne in mind. In severe cases with pus pockets a combined local and subcutaneous administration of the drug may be required to obtain the best results.

After a few injections of emetin the amebas disappear from the gums and subjective and objective improvement is quickly noted. The tendency of the gums to bleeding, usually so marked in this disease, is rapidly controlled by emetin. This apparent antihemorrhagic effect of the drug in pyorrhea alveolaris is as striking as it is in the dysenteric cases. In both instances it is probably due to the prompt destruction of the amebas in the tissues which, by their activity, are a source of constant irritation and inflammation as well as an important factor in spreading infection. Once these amebas are killed healing occurs very quickly and the bleeding stops. There is no proof[24] thus far that emetin exerts any influence on blood-pressure, coagulability of the blood, or the cell counts.[25] In spite of this the drug has been quite largely employed in the treatment of hemorrhages from many causes and organs. In three cases of hemoptysis the writer[26] was unable to observe that the drug possessed any antihemorrhagic qualities, and believes, therefore, that most of the favorable reports are due to the well-known tendency of hemorrhages to spontaneous arrest.

Very recently in five out of seventeen excised tonsils amebas have been demonstrated by Smith, Middleton, and Barrett. The exact role played by the amebas in such cases is not definitely determined. In any event they are a complicating factor and tend by their activity to keep up chronic irritation and prevent healing. The above-mentioned observers lay stress upon the fact that the amebas feed largely upon the accompanying bacteria, and in their bacterial phagocytic action they doubtless set free different endotoxins. The end results of this toxic absorption will therefore vary in their manifestations according to the kind of microörganisms

[23] Lyons, R., Emetin Hydrochloride in the Treatment of Amebiasis and Other Affections, read before Southern Medical Association, November 11, 1914.

[24] Flandin, Emetin in Hemoptysis, Soc. Med. des Hôp., July 18, 1913.

[25] Maurel (Bull. de l'Acad. de méd., March 24, 1914, cited from Prog. Med., December, 1914, p. 348) claims that emetin acts electively on smooth fibers and particularly on those of the bloodvessels, causing them to contract. This vasoconstriction explains, in his opinion, the influence of emetin on hemorrhage. On the other hand, Maurel states (Arch. de méd. et d'Anat. Path., May, 1914, xxvi, 3, p. 225) that the apparent beneficial action of emetin in arresting hemorrhage is all the more to be wondered at, seeing that experimentally in animals it has proved to have no action as a vasoconstrictor.

[26] Loc. cit.

ingested. In one of the nine clinical cases reported by the authors the patient suffered from a multiple arthritis. Amebas were found in the tonsils and also in the gums. Emetin in small doses apparently relieved the arthritic symptoms after the salicylates had failed.

That amebas may be found complicating or causing other pathological conditions is not improbable, but until this is shown to be the case the heterogenious use of the drug in all sorts of affections is hardly to be recommended, as it will tend to throw discredit upon one of the most valuable therapeutic agents we have at our command.

SUMMARY. The chief points brought out may be briefly summarized as follows:

1. Ipecac and emetin when taken by needle or by mouth act through absorption into the blood stream and exert their specific effect only on those entamebas within reach of the circulation, that is, in the tissues. Entamebas free in the lumen of the gut are apparently not affected by either the oral or subcutaneous use of emetin or ipecac.

2. It is not definitely known how or in what form ipecac and emetin are eliminated from the body, but there is some experimental evidence that the amebicidal principles of ipecac (emetin) when taken by mouth are not eliminated in the feces.

3. The failure of the emetin by needle to destroy the vegetative *Entameba coli*, a parasite simply harbored in the intestinal canal, argues against the elimination of the drug from the circulation by way of the large intestines.

4. Relapses are due to the survival of some of the entamebas probably through encystment. There is reason to believe that in the majority of relapses some of these cysts remain embedded in the tissues of the gut, only awaiting favorable conditions to become vegetative.

5. In the carrier state the entamebas are probably simply harbored in the lumen of the gut in the same manner as the coli, thereby causing no symptoms. The intestinal mucosa is in some way protected against the penetration of the organism.

6. Emetin is best administered subcutaneously. Small, repeated injections are to be preferred, as they are more rapidly absorbed and the effect is maintained. In severe cases emetin should be used intravenously.

7. The oral administration of emetin is not advisable because of the intestinal irritation that results. The whole drug is preferable for this route. For the same reason emetin is not suited for colonic irrigations.

8. In an ordinary case of amebic dysentery an average of one grain daily or less is sufficient. The duration of the treatment is from one to two weeks. Too large doses or too prolonged use of

moderate doses may cause a diarrhea or be responsible for its persistence. There is increasing evidence that large doses of emetin are not without ill effect.

9. In order to prevent relapses an intermittent form of treatment should be instituted in every case even though cysts are not found.

10. Emetin, subcutaneously and locally, has been shown to be practically specific in pyorrhea alveolaris.

11. The use of emetin in hemorrhagic conditions is entirely empirical and its value is questionable.

TREATMENT OF SCOLIOSIS.

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There are two principal forms of lateral curvature of the spine which present themselves to the practitioner's attention, (1) the functional or the static form, and (2) the rotary or the organic variety. So much attention has been given of late to the treatment of the rotary form that the consideration of the functional type has been largely neglected. Since many of the rotary cases have at some period been of the functional type, and have taken on the rotary form through neglect or inefficient treatment, the consideration of the functional form becomes a matter of paramount importance. In order to determine the presence of the primary form it is necessary to recognize the functional type of the affection and to distinguish it from the rotary or organic type. This can be determined by:

1. The history of the case. There are certain etiological factors which should always first be considered before undertaking the treatment of any case of scoliosis. The history should include the birth, whether natural or instrumental; if employed, the occupation; the age at the onset of the affection; any visual errors; the effect of puberty or of any antecedent illness which might have led to general debility, such as fevers, pulmonary affections, acute exanthemata of youth; the diet from birth, especially such as would tend to produce rickets; inherited tendencies, especially tuberculosis; the inheritance or acquisition of nervous affections, such as dystrophies, infantile paralysis, unilateral development; congenital defects of the spine; or the loss of a member from congenital absence, disease, injury; or finally the inequality of the

lower extremities from any of the many causes which produce this deformity.

2. The examination of the patient in Adams' position.

3. The recognition of the functional form from the lateral blending of the English.

Of the functional type several groups are classified according to their etiology, and these include the habitual, the true static, and the occupational.

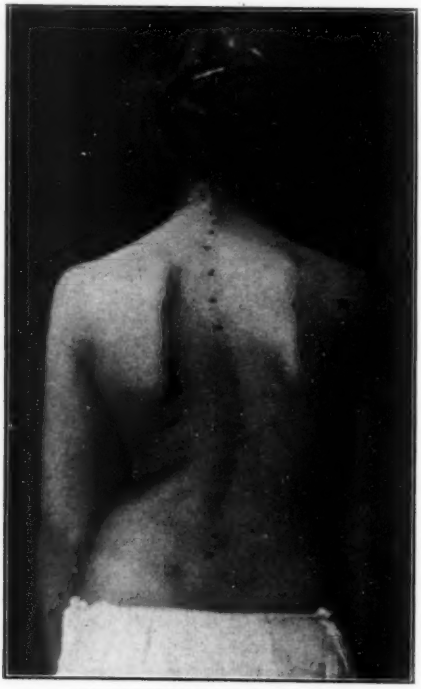

FIG. 1.—Right dorsal scoliosis.

The *habitual* results from partial or unequal use of the muscular system, the faulty positions being assumed either from carelessness or fatigue, as a single instance may be mentioned the scoliosis to be observed in artists' models that have become deformed from assuming certain positions for long periods of time.

In the *static* form there is an inequality resulting from alterations of one extremity. Whatever produces a shortening of one lower extremity produces an obliquity of the pelvis in the opposite direction, and a primary deviation of the lumbar vertebræ. This

may result from destructive changes in the articular structures, flat-foot, back-knee from ligamentous relaxation, etc.

As indicated by its appelation, *occupational* scoliosis results from oblique positions assumed during occupations. Lateral curvature in youth is specially liable to affect those whose work requires them to bear heavy burdens upon one side. The habitual is most amenable to treatment.

In order to recognize more accurately the functional form the organic must at once be clearly differentiated. These are the true rotary forms, and their diagnoses rest upon the following factors:

FIG. 2.—Severe double curve due to rickets.

(1) The Roentgen-ray examinations. (2) Examination in Adams' position, in which attitude the curve persists as a permanent deformity on the convex side. (3) By suspension, in which position the curve is only slightly affected.

Of the organic group some of the types of cases are amenable to correction by forcible methods of treatment. These are the cases of the functional type that have gradually become more severe, and to which rotation and torsion have been added, and in which the structures have become firm and unyielding, giving the so-called "fixed curves." The organic forms not amenable to treatment are

those due to infantile paralysis, to suprenumerary bones and enlarged processes, empyema, bone-softening, and rickets.

Treatment of the Functional Form. For many years this variety of scoliosis has been treated by orthopedic surgeons, with much success, by exercises and corrective measures. Many years ago the writer presented a method of treating these forms by a series of gymnastic exercises.[1] This method of treatment, thus advocated, has been used to the present time, and is still employed with much satisfaction in this type of cases, and to it has been added certain manipulations and mild forcible corrective measures which make it extremely valuable in the treatment of these secondary forms of scoliosis. The best results are obtained in private practice but where individual work can be substituted for class work the results in hospital cases are very gratifying. Systematically arranged these measures are as follows: (1) Development of weak muscles by exercises adapted to them individually or collectively; (2) slight over-development of the weak muscles; (3) uniform development of all the muscles; (4) employment of special movements to prevent relapse.

To successfully treat this class of cases it becomes incumbent upon the surgeon to discover the best voluntary position that can be assumed by the patient to correct the deformity and then in taking all the exercises in that position or in favoring that position in the use of all movements. Such a procedure of necessity leads to the development of the muscular structures, on the concave side of the deformity, and of the stretched or atrophied muscles on the convex aspect, these exercises to be continued or modified until slight overcorrection has been secured. Each case is a study in itself, and while individual sets of exercises are prescribed for certain curves, experience has amply demonstrated that certain combinations of exercises are best adapted and are capable of yielding the best possible results, in very many cases, that offer themselves for treatment. These exercises must be taken under the supervision of the surgeon, the trained instructor, or the masseuse. They are to be indulged in once a day, from thirty to forty minutes each; and two hours after or one hour before a meal. Massage is to follow, and afterward the patient must lie in the prone position or the keynote position, for a half-hour to an hour. The keynote position for right dorsal scoliosis (the more usual variety) is with the right arm extended sideways and the left arm elevated by the side of the head. These exercises are to be continued daily for six weeks, or tri-weekly for three months, and at two periods of the year, except during the menstrual periods and on Sundays. They are given three or four at a time by the surgeon until the whole series has been mastered, and should never be carried to the point

[1] International Clinics, 1898, vol. ii, eighth series.

of fatigue. Throughout the exercises normal breathing should be indulged in, and at the end of each exercise one or two full breaths should be taken. If other work conflicts with the course of treatment it is necessary to omit all duties, school-work, etc., so that the patient may conscientiously comply with the requirements as laid down by the surgeon.

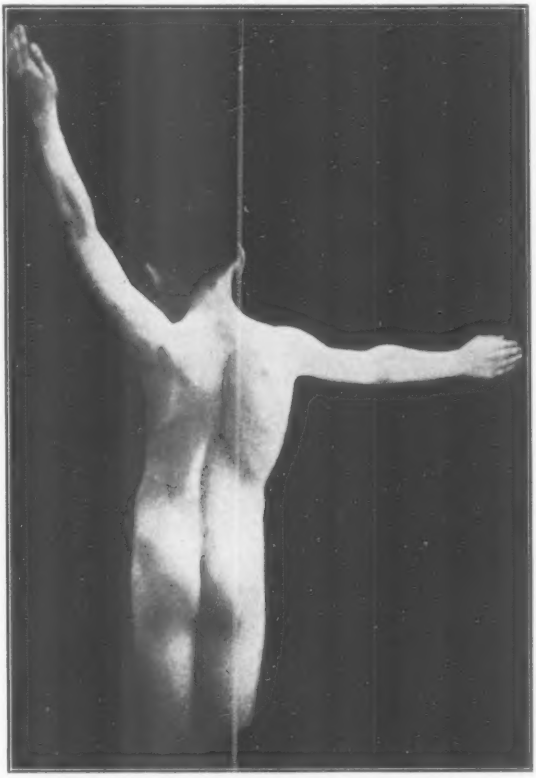

FIG. 3.—Right dorsal curvature. Key-note position.

The medical treatment should be directed by the family physician. He may build up the patient by the employment of tonics and remedial agents such as come within his province. Menstrual irregularities will be corrected as soon as the scoliosis is corrected. Flat-foot or any asymmetry in the lower limbs should engage the serious attention of the orthopedic surgeon as well as any injury to the hip or knee. Visual errors should be corrected by the ophthalmologist.

The special exercises in right dorsal scoliosis, which is the more common form (the treatment for left dorsal scoliosis being just the reverse), are as follows: (1) Best standing position: head up; abdomen in; chest *up* and *forward;* weight on balls of feet; (2) keynote position, which is, left arm upward, stretch; right arm sideways, stretch; (3) same as (2) with "trunk forward, bend;" (4) same as (2) with "trunk to right, bend;" (5) same as (2) with "trunk diagonally forward, bend;" (6) same as (2) with "heels raise;" (7) same as (6) with "knees bend;" (8) same as (2) with "right foot outward, fall out."

Additional exercises should be given to correct the irregularities in the lower extremities and to obliterate the secondary lumbar curve.

After the curves have been overcorrected, bilateral exercises must be used for the symmetrical development of the body. These may selected from the Swedish exercises or combined, so as to bring into play all the muscles of the body, by employing the following eight exercises, arranged by Dr. Keating and myself: (1) "Neck firm;" then "heels, raise;"[2] (2) "neck firm, trunk to left and right twist;" (3) "arms upward, stretch;" then "trunk to the left and right, bend;" (4) "arms upward, stretch; "then "trunk forward, bend;" (5) "right (or left arm) upward stretch;" then "right (or left) foot outward, fall out;" (6) "arms upward, stretch;" then "right (or left foot) outward, fall out;" then "trunk twists toward the side, corresponding to the forward foot;" (7) "arms sideways, raise;" "right (or left) foot forward, fall out;" (8) "arms upward, stretch;" "heels raise;" "knees bend."

Apparatus. In the treatment of these cases, certain apparatus will be found valuable, especially the high plinth of the Swedes, stall bars, and certain stretching apparatuses and appliances, such as the lateral suspension apparatus of Redard, Beely and Lorenz, which will be found invaluable. Suspension may be facilitated by the use of rings, various kinds of ladders, trapeze, etc.

Braces. In the treatment of mild cases of functional scoliosis, braces are seldom necessary, but a light corset-support, of the Shaffer type, as modified by the writer, is useful as a reminder to the patient, to assume a correct position, and offering a slight support to the patient during the intervals of exercise and recumbency. It should be made of light steel or duralamin,[3] and may be incorporated into a corset or worn under the corset. It consists essentially of a waist band, steadied by vertical pelvic bands, from which is built up a crutch, beneath the depressed shoulder, and a pressure-pad over the deformity.

[2] Cyclopedia of the Diseases of Children, Keating, year, vol. iv, p. 318.

[3] Duralamin is the new orthopedic metal, employed in the arts, made by the manufacturers of the celebrated Maxim guns. It is employed in the construction of air ships and submarines, and was introduced by the writer to the notice of the Medical profession (Orthopedic Transactions, September, 1913). It is almost as strong as steel, and but one-third as heavy, and is more stable than aluminum.

HISTOPATHOLOGY OF CALCIFICATION OF THE SPINATUS TENDONS AS ASSOCIATED WITH SUBACROMIAL BURSITIS.

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Under the title "Prevalent Fallacies Concerning Subacromial Bursitis; its Pathogenesis and Rational Operative Treatment," Brickner has described[1] his observations, surgical and radiographic, of calcareous deposits in and upon the supra- and infraspinatus

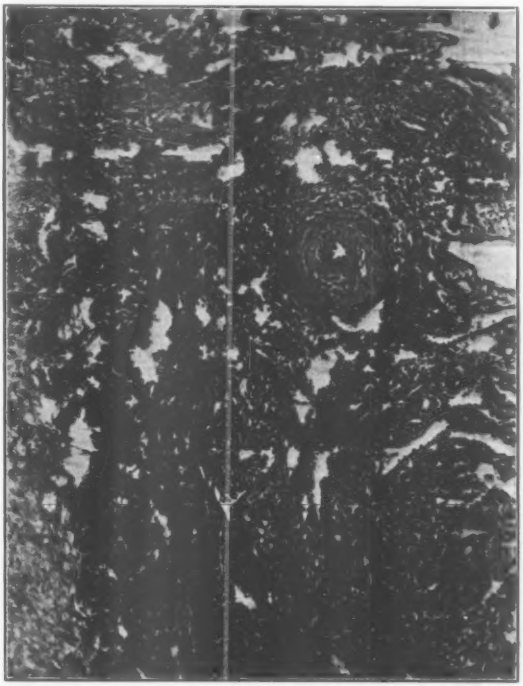

Fig. 1.—Case 1. Showing intratendinous formation of young granulation tissue and formation of new bloodvessels. To the left, a narrow zone of older organized connective tissue.

tendons, associated with adhesive subacromial bursitis. The following is based upon the histological study of portions of diseased tendons in four of his cases.

[1] Amer. Jour. Med. Sci., March 1915, cxlix, 351.

CASE I.—Female, aged forty-five years. Operation upon the sixteenth day after indirect trauma. Fresh adhesions in and ecchymosis of bursa; yellow, semiliquid calcareous deposit overlying and within laceration of swollen supraspinatus tendon; infraspinatus infiltrated with blood.

Pathological Examination (Figs. 1 and 2). Section shows a crescentic mass of tissue. Covering the entire convex border is a narrow zone of fairly loose connective-tissue fibers—a comparatively sparse number of large, long spindle-shaped cells of the connective-tissue type, a fair sprinkling of round cells, a few red blood cells,

FIG. 2.—Case 1. Necrotic tendon lying within granulation tissue containing small discrete deposits of lime.

a few thin-walled bloodvessels. This tissue represents a fairly well-organized granulation tissue.

Within this zone and filling the cavity of the crescent is a mass of tissue appreciably more cellular. The general appearance is that of an early form of granulation tissue. The predominant cell type is the round or plasma cell. There are a small number of spindle shaped connective-tissue cells and a few old and many newly formed bloodvessels. This tissue is abundantly infiltrated with red blood cells, most of which show degeneration changes, showing that the hemorrhage antedates the operation. The few old bloodvessels are small in size, and have thickened walls; this thickening

is largely due to swelling of the intima. The newly formed blood-vessels are irregular in shape and size, and consist mainly of clefts or spaces within the granulation tissue lined by a distinct and uniform row of endothelium.

Upon the innermost aspect of this area of young granulation tissue there are finely granular amorphous masses of necrotic tissue. While this necrotic tissue stains diffusely with eosin, here and there

FIG. 3.—Case 2. Well-organized granulation tissue springing from a tendon that has undergone extensive hyaline degeneration. Small discrete lime deposits lying within the tendon and in the granulation tissue. Here and there a foreign body giant cell.

are scattered discrete sand-like particles, that stain blue with hematoxylon, indicating a lime reaction. The greater part of this necrotic tissue lies loosely within the cavity of the crescent; a much smaller portion is still in direct continuity with the adjacent granulation tissue.

Epicrisis. This section reveals substantially two stages of granulation tissue: an outer, the older, which may be interpreted as representing the wall of a focus of inflammation; and an inner,

a more recent variety. In addition, there is within the centre of this focus necrotic tissue. This has undergone partial calcification.

Diagnosis. Necrosis of tendon with partial calcification and young granulation tissue.

CASE II.—Indirect trauma four or five months previously. Male, aged thirty years. Extensive adhesions in bursa; finger-nail-sized, gritty, yellow deposit entirely within supraspinatus tendon about 5 cm. from its insertion.

Pathological Examination. Sections show two different masses (Figs. 3 and 4). The first and larger consists of an irregular mass of tendon tissue continuous with a large area of granulation tissue.

FIG. 4.—Case 2. Tendon tissue that has undergone extensive hyaline degeneration and calcification.

The tendon consists of firm fibrous longitudinal bands of connective-tissue, portions of which show hyaline degeneration. Only a small area of tendon fiber is present; the rest have undergone extensive calcification. The calcification is present either in the form of discrete, sharply circumscribed, sand-like masses embedded, as it were, in a cavity within the tendon; or as diffuse finely granular masses, shading imperceptibly into the surrounding tissue structure; or as finely granular amorphous material lying within the tendon or the granulation tissue.

The granulation tissue is richly cellular, almost sarcomatous in appearance, and consists of large oval or spindle-shaped cells

with a finely fibrillar intercellular connective-tissue. There are many delicately walled newly formed bloodvessels. A few giant cells are present, some in relation to the lime granules, some not. They are all probably so-called "foreign body" giant cells.

The second and smaller mass consists of hyaline tendinous tissue which has undergone almost complete calcification. The lime deposit consists of finely granular masses, either within the tendon or upon its surface.

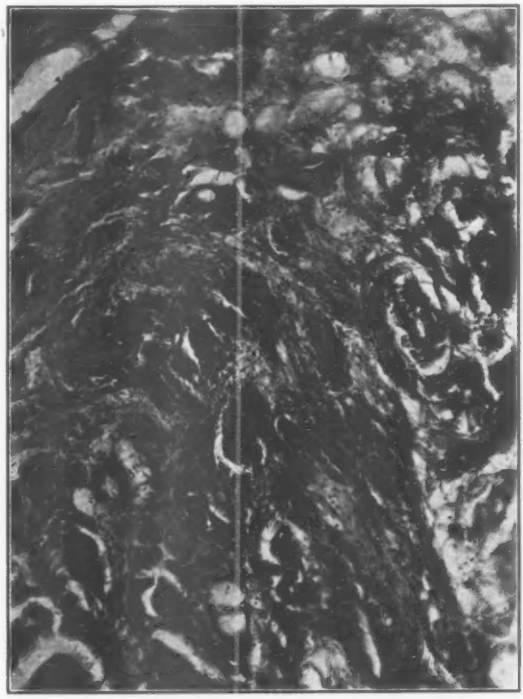

FIG. 5.—Case 3. Tendon bundles separated from one another by extensive scar tissue.

Epicrisis. A tendon that has undergone extensive hyaline degeneration and calcification. There is manifest necrosis with secondary calcification of the tendon. In addition, there is a comparatively early form of granulation tissue.

Diagnosis. Chronic tendinitis, with necrosis, hyaline degeneration, and calcification, and the formation of granulation tissue.

CASE III.—Chronic (one and a half years). Female, aged about forty-five years. No history of trauma. Persistent "brachial

neuritis." A few fine adhesions in bursa; small, dry, gritty, yellow-white lime deposit, entirely within infraspinatus tendon near its insertion.

Pathological Examination. With the low objective the section shows essentially a mass of tendon tissue encircling a cavity which contains necrotic detritus (Figs. 5 and 6). The tendon tissue consists of dense strands of fibrous tissue which is grouped in longitudinal strands or bundles. Between many of these bundles is loose cellular tissue, consisting of coarse fibrous tissue, many spindle-shaped connective-tissue cells, and a small number of delicate-walled bloodvessels. In some areas the tendon bundles

FIG. 6.—Case 3. Wall of cavity within tendon containing necrotic tendon tissue.

have undergone hyaline degeneration. The cavity within the tendon contains a finely granular amorphous mass of necrosed material which in part lies loosely within the cavity and in part is continuous with the fibrous wall of the cavity. No calcification is present, although Dr. Brickner assures me that much gritty material was found at operation. The lime must have been shaken out of the specimen during manipulation.

Epicrisis. This section represents a tendon between the bundles of which firmly organized tissue has formed. The tendon bundles have in part undergone hyaline degeneration. Within the tendon is a cavity containing necrosed material.

Diagnosis. Chronic tendinitis with hyaline degeneration.

CASE IV.—Acute. Male, aged about sixty years. Operation seventeen days after direct injury. Well-developed adhesions in bursa; two discrete white powdery deposits in supraspinatus tendon.

Pathological Examination. Sections reveal a thin rind of tendon tissue enclosing a cavity containing finely granular necrosed material. Within the tendon tissue are extensive areas of necrosis, most of which take the lime reactions with hematoxylon. The necrotic material within the cavity also shows extensive areas of calcification. In no specimen was the slightest reactive tissue noted, in the form of round-celled infiltration, granulation tissue, or the formation of new bloodvessels.

Diagnosis. Necrosis and calcification of tendon.

SUMMARY. The first three cases exemplify three stages of a lesion that may be termed "tendinitis." The common factor is the formation within and around the tendon fibers of granulation tissue which corresponds in a general way, according to morphological criteria, with the duration of the illness. We find, accordingly, a progressive organization of the reactive inflammatory tissue in and around the necrosed portions of the tendon, so that a mere round-celled infiltration with early formation of bloodvessels in the first case becomes a scar-like tissue, with fully developed bloodvessels in the third. The last case shows no reactive tissue around the dead portions of the tendon, although the duration of illness was practically the same as in the first case. The only way we can account for this absence is the age of the patient, at which time the reaction forces of the body are notoriously deficient.

Necrosis. Another common factor in all four cases is the presence of necrotic tissue. It has the same morphological appearance in all, namely, a finely granular, amorphous, and completely acellular mass. In Cases I, II, and IV this necrotic tissue is more or less calcified. Topographically the necrotic tissue has two relations: either in direct continuity with the tendon, or with a greater or smaller zone of granulation tissue intervening.

The necrotic tissue can have only two sources: (1) the degeneration of the blood and serum consequent upon the primary trauma; (2) the breaking down by coagulation necrosis of the tendinous structures. The first origin can obviously be excluded for the following reasons: (*a*) There is no blood pigment; (*b*) the appearance of the tissue is too homogeneous and plastic to arise from a fluid origin; (*c*) the continuity between the necrosed area and the surrounding solid tissue is a gradual one, so that it is impossible to determine a sharp definition between the well-preserved and the necrotic areas. Were the necrosis of fluid origin we should expect a cyst-like cavity. I conclude, therefore, that the necrosis arises from actual death of tendon. The explanation of the necrosis is

obvious. The blood supply of a tendon is notoriously meager. The tendon bundles proper have no blood supply. Whatever bloodvessels the tendon contains are present only in the connective-tissue left between the tendon bundles (Stöhr), and these are small in size and number. It is, therefore, readily understandable how a trauma, however slight, may interfere profoundly with the blood supply of a given area of tendon and thereby cause necrosis.

Calcification. Lime is found in Cases I, II, and IV. In Case III Dr. Brickner assures me that he found gritty masses at the operation. The failure to find lime microscopically, therefore, may be regarded as accidental, due, in all probability, to the fact that the lime deposit was shaken out in the subsequent manipulation of the specimen.

The lime is present in three forms: (1) as small sand-like particles within the necrosed tissue; (2) as diffuse massive calcification of the necrosed tissue; (3) as isolated discrete and sharply defined nodules embedded within the tendon or the granulation tissue. Furthermore, Brickner reports calcification in some cases upon the surface of the tendon, in the form of a thick, white, gritty material, associated with a minute tear of the tendon. He has also found at operation, and by Roentgen-ray, multiple deposits in the tendon, sometimes at a considerable distance from its insertion. In some cases the shadow-forming deposit is quite liquid, and this occurs in early as well as old cases, in extra- as well as intratendinous deposits.

What is the pathogenesis of this calcification? At the outset it is necessary to settle the question whether these tendinous calcifications are due to injury of the humerus, by the statement that neither Brickner nor any other observer has ever seen any direct connection of the deposit with the bone, either by Roentgen rays or at operation.

The pathogenesis of calcification within tendons is governed by the same conditions that apply to abnormal calcifications in other parts of the body. It has been definitely established that calcification only occurs in dead or inert tissue, that is, tissues that have no blood supply. It never occurs in tissues whose blood supply is abundant. Familiar examples of calcification in necrosed tissues are those in caseous tubercles, atheromatous plaques, old abscesses, infarcts, and old sebaceous and dermoid cysts. Furthermore, calcification has a peculiar predilection for connective-tissues that have undergone hyaline degeneration, which also is merely a form of necrosis. This is commonly noted in fibromyomata of the uterus of long standing. I have also noted this phenomenon in the hyaline corpora albicantia of the ovary; in the wall of a chronically inflamed tube; in old pleuritic thickenings; in the walls of hydatid cysts; in old scars, etc. Furthermore, it is an interesting observation that wherever we find a deposit of lime, we are apt, at the same time, to find partial ossification of the tissues. The

conditions under which ossifications form after calcification are not precisely understood, but they probably depend upon two factors: (1) a sufficient period of time and (2) the formation of a reactive blood supply. We predict, therefore, that an extensive study of calcified tendons will sooner or later discover an instance of ossification. This point will again be discussed in greater detail.

Causation of Early Calcification. Brickner[2] calls attention to the remarkably early appearance of the calcification in these cases. In addition to the first and fourth cases, in which the lime deposit was demonstrated, roentgenographically, upon the tenth and eleventh days respectively following the injury, Brickner has found the deposit by roentgenography as early as twenty-four hours and five days after trauma.

Now, in all the instances of pathological calcification that we have considered it has been generally accepted that the deposition of lime occurs only when the necrosis is of long standing. Calcification of a tissue, in other words, is generally regarded as indicating chronicity of the lesion. How, therefore, are we to account for the very early calcification noted in these cases?

It seems to me that sufficient explanation of this phenomenon is found in the observations upon experimental calcification. Litten[3] and Lick[4] found lime microscopically in necrosed portions of the kidney, one day after ligature of the renal artery. Especially significant for our purposes are the observations of Schujeninoff,[5] who found calcification of the muscle fibers both in man and in animals one and a half days after the suture of a divided muscle. The lime in every instance was near the suture line, and the affected muscle fiber was the seat of colloid degeneration. Schujeninoff believed that the calcification was due to interference with the circulation by the ligation of small bloodvessels. I have frequently seen calcification of necrosed portions of malignant growths when the duration of necrosis could be reasonably reckoned in terms of days.

Strangely enough, the repeated observations upon experimental healing of tendons fail to throw any light upon the problem of the early incidence of calcification in the spinatus tendons. Studies upon the injury and repair of tendons are numerous enough, the more comprehensive being those of Palla,[6] Seggel,[7] and Yamagiva.[8] I have studied the extensive protocols of these writers carefully, and in not a single instance was calcification of the tendon noted. The absence of calcification is puzzling, and can be accounted for only by the fact that the tendo Achilles, exclusively employed for experimental purposes, presents some peculiar biological proper-

[2] Loc. cit.
[3] Ztschr. f. klin. Med., 1880, v. i.
[4] Arch. f. klin. Chir., 1908, lxxxv, 118.
[5] Ztschr. f. Heilk., 1897, xviii, 79.
[6] Beitr. z. klin. Chir., 1909, lxiii, 644.
[7] Ibid., Chir., 1903, xxxviii, 342.
[8] Arch. f. Path. Anat., Virchow, cxxxv, 308.

ties that do not predispose it to calcification. In order to satisfy ourselves upon this point, we propose, at some future date, to repeat these experiments upon the spinatus tendons.

At all events, there is already ample evidence in certain tissues, at least, that calcification in necrotic tissue occurs earlier than is generally believed. In all probability the early or late incidence of calcification depends upon peculiar predilections of certain tissues, due to chemical affinities the nature of which has not been precisely determined (Adami).[9] This will explain why calcification occurs oftener in some tissues than in others. Wells[10] accounts for the greater frequency (in his experience) of calcification in the lungs, stomach, and kidneys by the fact that these organs have an acid secretion which precipitates carbonate of lime. This contention is hardly tenable in view of the fact that some of the commonest lime deposits arise in tissues that are constantly bathed in alkaline juices, for example, arteriosclerosis. To explain the early calcification in tendons, we suggest that perhaps it is the collagen, present in the tendons, according to Gies and Buerger,[11] to the extent of 37 per cent., that acts as the lime precipitant. This suggestion arose from the observations of Schujeninoff,[12] who showed that the muscle fibers in which lime deposition occurred were in a state of colloid degeneration—a condition chemically allied to collagen; and, furthermore, by the affinity of cartilage (which is also rich in collagen, (Hammersten[13]) for calcification.

Maturity of the patient is unquestionably a large factor in determining calcification of tendon, and, indeed, of other tissues as well. Calcification is extremely rare in children and youth, and becomes progressively more frequent as age advances. This explains why subacromial bursitis with calcification of the spinatus tendons has never been observed in the young.

Previous Pathological Studies upon Calcification of the Spinatus Tendon. As far as we are aware, no previous systematic study has been made of the pathogenesis of the lesion underlying the symptom-complex embraced under the term "subacromial bursitis." There are only two pathological reports upon excised portions of tendons, that of Wright, in one of Codman's[14] cases and that of Wrede.[15]

Wright's report was "microscopic examination of the material from your case of 'sub-deltoid bursitis' shows the following: The main constituent of the material is a coarse, dense, fibrous tissue. Associated with this is a looser connective-tissue in which are enclosed bloodvessels and a good many cells of the lymphocyte

[9] Principles of Pathology, Philadelphia, 1914.
[10] Arch. Int. Med., vii, 721.
[11] Amer. Jour. Physiol., December, 1901.
[12] Loc. cit.
[13] Text-book of Physiological Chemistry, Trans. from 7th German ed., 1911.
[14] Boston Med. and Surg. Jour., 1908, clix, beginning October 22.
[15] Arch. f. klin. Chir., 1912, xcix, 259.

series. The coarse, fibrous tissue in some places contains more fibroblasts than elsewhere, and may therefore be considered to be in process of growth at these points. In a few places it is necrotic, and it contains few bloodvessels. I can not find any evidence of tuberculosis. The material seems to me to show a slow, productive inflammatory process combined with degeneration and necrosis similar to the process observed in the heart valves in some cases of chronic endocarditis."

Wrede's case: Man, aged seventy-six years, who had suffered for one year following a trauma. At operation a deposit within the supraspinatus tendon was found. From this portion a small piece was excised. The tendon was found necrotic with deposition of lime. In addition there were granulation tissue and giant cells. These findings, therefore, correspond to our own. Wrede enters into a prolix discussion of the etiology of the malady, and finally assumes a non-committal attitude.

Analogy of the Lesion to Other Pathological States of Tendons. Calcification of the spinatus tendons, following so soon after trauma (the etiology described by the more extensive observers of this malady, Brickner and Codman), has, as far as I am aware, no precise analogy in human pathology. This singularity is especially striking when we consider that the trauma in most of the cases is slight or trivial, merely sufficient, as Brickner and Codman declare, to jam the spinatus tendons between the head of the humerus and the acromion process. The thought obviously suggests itself, Why are other tendons, such as the tendo Achilles and those around the knee and elbow which are more frequently subjected to trauma, free from such calcification? The answer is that such calcifications probably do occur, although the pathological proof is thus far lacking.

Since the introduction of the Roentgen rays, shadows in tendons, especially in the neighborhood of joints, are a frequent finding. As instances, we cite the not uncommon calcification or ossification in the tendo Achilles arising in continuity from the posterior aspect of the os calcis (Höring,[16] Jacobsthal,[17] Haglund,[18]), but sometimes isolated within the tendon (Blencke,[19] Finney,[20]); also to the frequent ossification of tendons around joints following sprain or fracture, for example, the triceps (Engelbrechtson,[21] Fragenheim[22]), brachialis anticus (Tyson[23]), adductor longus (Boyd,[24] Whitelock[25]), obliquus externus (Charles[26]), quadriceps femoris (Bähr[27]), gastrocnemius

[16] Deutsch. med. Wchnschr., 1908, xxxiv, 175.
[17] Arch. f. klin. Chir., lxxxviii, 146.
[18] Ztschr. f. orthop. Chir., xix, 457.
[19] Ibid, 1908, xx, 363.
[20] Quoted by Binnie, Keen's Surgery, vol. ii.
[21] Railway Surg. Jour., 1911–1912, xviii, 320.
[22] Med. Klinik, 1909, v, 278.
[23] British Med. Jour., April 16, 1910.
[24] Clin. Jour., London, 1897, x, 186.
[25] Sprains and Allied Injuries of Joints, London, 1909.
[26] British Med. Jour., 1912, i, 949.
[27] Quoted by Engelbrechtson.

and deltoideus (Whitelock[28]). The cases of so-called "riders' bone," *i. e.*, formation of bone within the tendons of the adductors of the thigh, and "drill bone," in the insertion of the deltoid, probably also belong to this group of traumatic "ossifications" of tendons. These citations prove that traumatic "ossifications" do occur, although by no means commonly. I have purposely cast doubt upon the validity of the osseous formation by the use of quotation marks for the reason that, with the exception of the case of ossification of the tendo Achilles, reported by Jacobsthal, the pathological proof of the presence of bone is entirely lacking. It is by no means proved that some of the shadows reported as bone by various observers may not have been those of lime concretions.

Whether these shadows are of lime or bone is, for our purposes, a matter of indifference, for the reason that, as most pathologists have agreed, calcification always precedes abnormal ossification. These shadows at some stage of the process must have been those of pure lime deposits. The earlier stages of bone formation are precisely those that we have described in our tendon specimens, namely, death of tissue with calcification. I have never, nor, as far as I am aware, has anybody else, seen an area of ossification occurring *de novo* in normal tissue.[29]

This postulate leads us to predict, as I have said before, that when more of these calcified spinatus tendons are examined, bone will sooner or later be found.

The demonstration, therefore, that calcification always precedes ossification removes whatever doubt may have arisen as to the validity of the analogy between the traumatic calcification of the supraspinatus tendon and the supposed bony lesions that we have enumerated.

The mere demonstration of an analogous traumatic lesion of the tendons by no means accounts, however, either for the peculiarly common or for the early incidence of calcification of the spinatus tendons. The lesions in the other tendons to which I have referred are infrequent, and the manner of the process indicates that the calcification must have come rather late upon the trauma. The lesions in the spinatus tendons, on the other hand, are comparatively common, as proved by the experience of Brickner, who has seen over twenty cases within the last two years. The early and common incidence appearance of lime in these cases has no precise counterpart, and neither of us is able to submit a satisfactory explanation. We hope to be able to later.

[28] Loc. cit.

[29] I have summarized the entire subject of the histogenesis of ossification in a paper shortly to be published, entitled, "The Relation of Angiogenesis to Ossification." In passing, the manner whereby a mass of lime is converted into bone is an interesting process, and analogous in its details to normal endochondral or membranous ossification. Furthermore, I shall show that the development of blood-vessels forms the keynote to the interpretation of the entire process.

REVIEWS

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Vol., IV; Number 1 (February, 1915); pp. 185; 41 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THIS publication inaugurates its fourth year with the query by Dr. Murphy: What is an intestinal fistula? The answer is included in a diagnostic talk followed by four illustrative cases, with comments. The possible sources of intestinal fistulas are mentioned in a table three pages long. The various locations of appendicular abscesses according to the position of the appendix, are shown in seven cuts taken from Dr. Murphy's article in Keen's *Surgery*. Dr. Murphy bemoans his inability to find a term more expressive of his opinion of the "expectant treatment" for appendicitis than the *mañana* method, or *dolce far niente*.

On page 26 the intern was right and Dr. Murphy wrong about the omission from the history of the patient's knowledge of his temperature. On the next page, in speaking of end-to-end anastomosis by the suture method, Dr. Murphy refers to the "Lembert" stitch. It is probable that he meant a Dupuytren stitch, which is the one usually employed in this operation, because it takes less time for insertion.

In discussing aneurysms on page 64, Dr. Murphy is in error when he describes Hunter's treatment as "a double ligation, above and below the sac." John Hunter's method was that of proximal ligation far from the sac, as is shown by his historical ligation of the superficial femoral artery in the canal that bears his name for popliteal aneurysm, in December, 1785. With the exception of turning out the clots, Dr. Murphy's definition corresponds to the treatment of Antyllus. The second table in the book gives a classification and statistics of aneurysm.

In Dr. Mix's discussion of the case of division of the brachial plexus, he overlooks the fact that the brachialis muscle is supplied in part by the musculospiral nerve. A discussion of supraclavicular subcutaneous lesions of the brachial plexus not associated with skeletal injuries and occurring between the transverse processes and the clavicle, of which there are about twenty-one cases on record, is conspicuous by its absence, and might well have been

included. We doubt that the tendons of the pectoral muscles could be cut at a point corresponding to the middle third of the clavicle.

A series of illustrations shows Dr. Murphy's technique of inserting an intramedullary splint into a fractured tibia. The open reduction of a posterior luxation of the spine at the second lumbar vertebra is particularly interesting. In discussing a case of old compound fracture of the malar bone, Dr. Murphy says: "The trifacial is chiefly the sensory nerve (of the face), although it must not be forgotten that it also contains the motor nerve supply to the masseter muscle." Why were the temporal and external and internal pterygoids not included? In discussing a case of ununited birth-fracture of the clavicle in a boy, aged nine years, the statement is made that bone transplantation is out of the question. An inlay bonegraft inserted into the anterior surface could not have been included in this assertion. A statement worth emphasizing is: "Remember that, as a rule, a Lane plate should not be used where there is a failure of union." The talk on carbuncle of the arm is very valuable. In speaking of lip carbuncles, ligation of the facial vein high up to prevent thrombophlebitis extending into the ophthalmic vein and cavernous sinus is not mentioned. The remaining cases include plastic work on thumbs, plating of a fractured femur, and gangrenous appendicitis.

P. G. S., Jr.

Arteriosclerosis: A Consideration of the Prolongation of Life and Efficiency after Forty. By Louis Faugeres Bishop, A.M., M.D., Clinical Professor of Heart and Circulatory Diseases, Fordham University School of Medicine, New York City. Pp. 383; 11 plates, and 25 figures in text. London: Oxford University Press, 1914.

This volume comes to us in the usual good dress of the Oxford medical publications. Its contents survey from every angle this disease of ever-increasing modern interest. Twenty-one chapters take up arteriosclerosis, discussing etiology, symptoms, prevention, nursing, treatment, blood-pressure, angina pectoris, life insurance, chemistry of the proteins, the prolongation of life in arteriosclerosis, and so forth. Much emphasis is laid upon protein sensitization as a cause of this malady, while the liberal protein diet is the subject of discussion in many paragraphs. The book is written in a very entertaining style. It leaves the impression that its author is perhaps a trifle overenthusiastic and that he has resorted to some unnecessary repetition in order to fill out the pages. For example, of the fifty-four pages devoted to the chapter on diet in arteriosclerosis, forty-two are devoted to cheese as an article of food. Yet the book is, on the whole, very interesting, especially so in the portions which touch upon the personal experiences of the author.

He is apparently a man who is up to date and abreast with the times. The notable feature of the work is the impressive emphasis laid upon the somewhat belated recognition by physicians that arteriosclerosis is a disease and not a lesion, that fibrosis or calcification in the arteries is not essential to its diagnosis, that such arterial changes may exist without evidence of the clinical condition whatever, and that ordinarily these vascular changes are accompanied by changes in the heart and other organs, thus frequently causing evidence of the disease entirely outside of the bloodvessels. While the book at times lags in interest, it shows all the earmarks of a thorough familiarity with the subject under discussion. It is refreshing and stimulating. It is food for thought, and seems to point in the proper direction. T. G. S.

PRAKTIKUM DER CHIRURGIE: EIN LEITFADEN F. AERZTE UND STUDIERENDE. Von DR. D. NORDMANN, Oberärzt der 2. chirurgischen Abteilung des Auguste Viktoria-Krankenhauses Berlin-Schöneberg. 1. Teil, allgemeine Chirurgie. S. 216, mit 90 teils farbigen Abbildungen. Berlin und Wien: Urban & Schwarzenberg, 1915.

WRITTEN at the request of colleagues, Nordmann briefly presents points essential to every-day surgery, dedicating the volume to his teacher, Werner Koerte. The work is based upon his experience of many years as Assistant in the Municipal Hospital at Urban-Berlin.

In a brief introduction Nordmann sums up the qualifications of a modern surgeon, saying very properly that he must be grounded in small details, and that while he must not cling to the old too long, yet he must not be too ready to adopt the new.

In going over the book carefully the reviewer noted numerous differences in the details of surgical technique as carried out in Germany, from the American methods. Errors of omission and commission were relatively common, a few of which are subjoined.

In carcinoma of the breast, the etiological influence of a single, large trauma should be pointed out. Paget's disease of the nipple, or epithelioma of the lactiferous ducts, as well as Virchow's carcinoma mastitoides, should not have been omitted. The etiological significance of a single severe trauma in sarcoma is not mentioned. Coley's fluid is not alluded to. In pseudoleukemia the role of the diphtheroid bacillus is not annotated. In the differential diagnosis of lipoma, especially of the soft variety, cold abscess should receive its share of attention. Radium is not referred to as the best means of treating warts, nor of certain angiomata. No mention of Ludwig's angina is made throughout the book—a rather serious omission.

On the whole, the enchiridion forms a safe and reliable guide for the general practitioner who does surgery, as well as for the surgical neophyte. The medical aspect receives due prominence, and the principles of therapeutic rest, so ably inculcated by Hilton, are properly emphasized. There is a pleasing interspersion of illustrative cases throughout the volume. P. G. S., Jr.

A Text-book of Histology. By Frederick R. Bailey, A.M., M.D. Fourth revised edition; pp. 644; 384 illustrations. New York: William Wood & Co., 1915.

This is a book written for the instruction of students of normal histology, to be used in connection with laboratory work. That it has now reached its fourth edition shows that it has proved itself adapted for this purpose. The book is subdivided into four parts: Histological technique occupies forty pages, and the general account of the cell, twenty pages. The tissues are considered in eighty pages and the systems of organs in three hundred and forty pages. Over a third of this latter part is devoted to the account of the nervous system, which is written by a separate author, Dr. O. S. Strong, in a thorough manner. In each chapter, besides the description of the mature tissues, separate paragraphs are devoted to development, special technique, and general references for further study. The index is unusually complete. For illustrations, the author has adopted the easy method of selecting, with due acknowledgement, illustrations which suited his needs, from existing text-books or journals. In its present edition the book should continue to be a useful and reliable guide to the study of histology.

W. H. F. A.

A Manual of Physiology, with Practical Exercises. By G. N. Stewart, M.A., D.Sc., M.D. (Edin.), D.P.H. (Camb.). With colored plate and 467 other illustrations. Seventh edition. New York: William Wood & Co., 1914.

Authors of text-books may be divided into two groups: those who fill the pages with dogmatic statements, and those who discuss the more important problems with their reader, as it were, giving him sufficient data to exercise his own judgment, to some extent at least. Dr. Stewart certainly belongs to the latter group in spite of the fact that the book is called a manual. Only too often the sole purpose of the manual is to prepare the student for an examination. This book, on the other hand, has as its sole function the

expounding of the subject of physiology in its present state of advancement. The poor or indolent student who, misled by the name, buys this book with the intention of "getting" the subject in examination form with the least possible effort will be disappointed. The subject of physiology is becoming more complex each year, and likewise each new edition of this work has become more involved. This is particularly manifest in the chapter upon internal secretions, in the discussion of the action of the pancreas, in the chapter upon respiration on the action of the respiratory centre; indeed, knotty problems are discussed with the reader in every chapter; but with a clearness of presentation and logic as to lend much interest to them. The interested student will not be repelled but fascinated. It is, indeed, a splendid book. The author possesses an exceptional tolerance for different views, but not those based upon insufficient data. This is seen when he refers to the reciprocal relation of the ductless glands, where he states, "but the premature attempts which have been made, in the absence of a sufficiency of exact data, to represent their mutual influence by crude schemata, have retarded rather than advanced our knowledge, and need not be referred to here." But one criticism can be made of this book and that is in regard to the practical exercises. They are entirely too incomplete to meet the requirements of a good medical school. E. L.

URINARY ANALYSIS AND DIAGNOSIS BY MICROSCOPIC AND CHEMICAL EXAMINATION. By LOUIS HEITZMANN, M.D. Third revised and enlarged edition. Pp. 345; 131 illustrations, mostly original. New York: William Wood & Company, 1915.

THE present edition of Heitzmann's treatise upon urinalysis conforms largely to the style and manner of presentation of the previous editions. Numerous changes have been made, however, in the text, so that the subject-matter has kept pace with the many advances made in the chemical analysis of urine, while in dealing with microscopical examination and more particularly with microscopical diagnosis, the author sets a pace which at times it is difficult to follow. Certainly if all the various types of diseases of the urinary tract could be as readily diagnosed by the examination of the centrifuged specimen as Heitzmann would have us believe, a great advance would be attained in the study of these disorders.

The book is divided into three parts dealing respectively with the chemical examination and microscopic examination of the urine and with microscopic urinary diagnosis. The first section presents admirably the various methods of chemically examining the urine which can be employed by any practitioner with only

a minimal amount of apparatus. The second part is notable for the splendid drawings, illustrative of all possible organic and inorganic, normal and abnormal, constituents of the urine seen microscopically. The third division deals with the diagnosis of lesions in the urinary system, and while much that is written here is most praise-worthy, it does seem, however, that it is stretching a point to claim that practically always the diagnosis, the duration of the disease, and the prognosis can be determined by the study of the type of casts, the character of the epithelia and the other urinary constituents seen under the microscope.

The book as a whole is a commendable piece of work. It does not attempt to delve deeply into the complicated depths of urinary examination but shows clearly how much may be learned from the data obtained by the careful study of the urine in an ordinary "routine examination." J. H. M., JR.

A MEDICAL DICTIONARY FOR NURSES. By AMY ELIZABETH POPE, Instructor in School of Nursing, St. Luke's Hospital, San Francisco, Cal. Pp. 288; 11 illustrations. New York: G. P. Putnam's Sons, 1914.

THIS book is of convenient size, bound in blue linen, uniform with the other books by Miss Pope. It is printed in clear type and on easily read paper. The definitions given are clear and show extensive reading and thought on the part of the author. For a dictionary of its size it is not sufficiently complete, nor is the space allotted to the various words evenly distributed. For instance, after the word *bath* there are about 1300 words; after syphilis about 300 words; whereas, many words in common use, such as, borborygmus or diverticulum, are not included. However, the definitions of the words given are clearly expressed. The work will be of value to the student nurse. M. V. S.

DIE MENSCHLICHE INTELLIGENZ UND IHRE STEIGERUNG. By DR. MED. A. LORAND. Pp. 416. Leipzig: Verlag von Dr. Werner Klinkhardt, 1914.

THIS is an interesting, if long, dissertation on the human intelligence and its development. Its text is divided into the various causes which have a tendency to influence thought. In the first division is discussed the influence of circulatory changes, glandular structures, the nose, climate, and general nourishment. In the second is discussed the intelligence of men and women and the

influence of sex. In the third the influence of such extraneous subjects as alcohol, syphilis, migraine, and the various glandular diseases, as myxedema, etc. In the fourth the influence of sun, heat, cold, and various hygienic measures. In the fifth chapter is taken up the discussion of rational thinking, its development, and particularly the method of its improvement. In the sixth is discussed memory and its systematic development, and in the next chapter rational mental work, in which there is an interesting discussion on the influence of parents on children and the method of studying children. Perhaps the eighth chapter is most interesting, for it takes up the method to be employed in the development of intelligence in children, and the last chapter is very constructive, it being concerned with hygienic measures to be adopted in various schools to obtain the best results.

As can be readily seen from the above skeleton it would be difficult to adequately review such a work as this. To anyone who is interested in the development of intelligence this book offers a great deal. To those who do not believe that all sickly children should be done away with, this book offers some hope, for it is interesting to learn that James Watt was so ill as a child that he was compelled to sit in the house and read most of the time. That Descartes was compelled to lie in bed for eleven hours, and thus began his philosophy. That Kant, Locke, Francis Bacon, Newton, and Pope were sickly while youngsters. That Haemholtz was a hydrocephalic child and Rousseau's birth cost his mother's life. Rosseau and Voltaire were neurasthenic. The author also makes the interesting statement that those writers whose work was fantastical were very large meat eaters. He quotes Dumas the elder and Victor Hugo as shining examples of this. It is interesting also that these sickly children lived to an old age, for Humboldt died at ninety, Kant at eighty, Newton at eighty-four, Locke at seventy-one, etc. It can be seen from this that this work makes interesting reading. T. H. W.

FEEBLE-MINDEDNESS: ITS CAUSES AND CONSEQUENCES. By HENRY HERBERT GODDARD, Director of the Research Laboratory of the Training School for Feeble-minded Boys and Girls, at Vineland, N. J. Pp. 599; illustrated. New York: MacMillan Co., 1914.

THIS book represents the work done in the Vineland Research Laboratory during the past five years, it being an attempt to discover the causes of feeble-mindedness. The histories of 327 cases are presented. It is only necessary to say each case was thoroughly worked up, the material having been selected, and as a consequence the conclusions drawn merit all the attention that can be given to them. Most of the book is taken up with the detail of these

histories, they being arranged as much as possible, according to whether or not the causes are probably hereditary, with neuropathic history, accident cases, those to which there was no assignable cause, and those which were unclassified.

The most interesting part of the work, of course, is that which concerns itself with the causes and theories of feeble-mindedness and the remedies. The most interesting fact brought out was that the chief cause is hereditary, 54 per cent. of the cases studied being included in this class, and in addition 11.3 per cent. being grouped under the probably hereditary class. Their conclusions regarding alcoholism were surprising. They consider only the drunkards. They conclude that alcoholism itself probably does not cause feeble-mindedness. This is contrary to the usually accepted view. They come to the conclusion that feeble-mindedness is hereditary, and that a child will at maturity have the average intelligence that its parents had, and that the inheritance of feeble-mindedness is in accordance with the well-known Mendelian law. They are not by any means certain of this, but their studies have forced them more or less to this conclusion. Only a small part of the book is taken up with practical applications. They point out what has so often been pointed out by others, that the State should recognize that paupers, criminals, and ne'er-do-wells are such chiefly because they are feeble-minded and that they should be treated as such. They deplore the fact that all the States do not take into consideration the training of such classes, but treat them as criminals, thereby only propagating this class and not really coming to any definite conclusion.

On the whole, this book is an excellent study of feeble-mindedness, and should be recommended to all physicians and laymen who are interested in this subject. T. H. W.

DEFECTIVE OCULAR MOVEMENTS AND THEIR DIAGNOSIS. By E. and M. LANDOLT, (Paris). Translated by ALFRED ROEMMELE, M.B., CH.B., and ELMORE W. BREWERTON, F.R.C.S. Pp. 99; 27 illustrations. London: Henry Frowde, Oxford University Press, Hodder & Stoughton, Warwick Square, E. C., 1914.

THIS small volume is based upon the data of anatomy, physiology, and pathology of the muscles, nerves, and centres. We miss some of the clearness we are accustomed to find in the writings of the elder Landolt. This is due to the condensation of so comprehensive a subject when dealt with in this way. It is not easy reading, but is an excellent *vade mecum* for a student who has a fair knowledge of the anatomy of the nerves and centres governing the ocular muscles. T. B. S.

LES PREJUGES EN ART DENTAIRE (PREJUDICES FOUND IN DENTAL PRACTICE). By DR. E. CHAREZIEUX, Director de l'Ecole Pratique de Stomatologie ou des Hautes Etudes Dentaires de Paris. Pp. 120. Paris: A. Maloine.

THIS is one of a series of small volumes dealing with certain fallacious ideas that have crept into the practice of various specialties of medicine. It deals with prejudices existing both in the minds of the dental profession and of the laity. The writer gives his views upon the use of local anesthetics, when a tooth should or should not be extracted, the relation of dental sepsis to general health, etc. It would seem that some of the prejudices to which attention is called are more imaginary than real, at least as applied to the dental profession in this country, where the people as a whole also are probably better educated as to the care of the teeth than in France. R. H. I.

BEHANDLUNG KOSMETISCHER HAUTLEIDEN (SCHÖNHEITSFEHLER). By DR. S. JESSNER; Sanitätsrat. Third Edition. Pp. 159; 11 illustrations. Würzburg: von Curt Kabitzsch, 1914.

THE writer takes up a considerable number of dermatological conditions in his compact little volume—"Treatment of the Cosmetic Skin Diseases." Jessner first refers to the changes in the integument that are found in the newborn; the so-called "mother's-marks," vascular and pigmented nevi, and also ichthyosis. Then the various other cosmetic skin diseases are discussed. The "snow" treatment, electrolysis, the galvanocautery, the Paquelin cautery, the Finsen light, the uviol lamp (Schott), the quartz lamp (Kromayer) are mentioned in reference to some of the various conditions. Various acids, mitin paste, and a considerable number of local applications are exploited. F. C. K.

SCROFULOSIS. By PROF. DR. G. CORNET, Berlin and Reichenhall. Translated from the Second German Edition, by J. E. BULLOCK, M.D. Second Edition. Pp. 515. New York: William Wood & Co., 1914.

THIS the second edition of *Scrofulosis* appears seven years after the exhaustion of the first edition. Such unusual delay makes the book indeed practically a new one in significance, as many previous observations have been placed on firmer ground and the opportunity

has arisen for the addition of much new material. By its means a speedy grasping of this voluminous subject is made possible.

We are shown that scrofulosis is the result of a local diathesis affecting principally the skin, mucous membranes, their immediately underlying tissues and afferent lymph paths (rather than a general diathesis) upon which an infection is implanted. The infection may be tuberculous, human or bovine in origin, or due to the pus cocci. The characteristics and prognosis of the various types are described and their relation to general and pulmonary infection shown.

Therapeusis in all its aspects receives generous space. On completion of the book one feels that he has at last a rational basis for his advance in this much befogged field. The exhaustive bibliography deserves mention. A. A. H.

AN ELEMENTARY STUDY OF THE BRAIN. By EBEN W. FISKE, A.M., M.D. Pp. 132; Illustrated. New York: The Macmillan, Co.

THE purpose of this small volume is to supply a simple laboratory manual for the student beginning a study of the brain.

It contains several good features. The subject is treated from the biological standpoint, the first few chapters being devoted to phylogency and ontogeny. An attempt is made throughout the work to show the physiological and psychological aspects of the various parts described. S. L.

AIDS TO TROPICAL HYGIENE. By Major R. J. BLACKHAM, D.P.H. (Lond.), R.A.M.C. Pp. 187. New York: William Wood & Co.

THAT wonders in sanitation have been accomplished in Panama and other tropical localities is common knowledge, but except in the vaguest way, just how this has been done is not generally known.

In this book the problem of making a tropical country habitable for white men is taken up and the solution evolved.

Such topics as water supply, food, clothing, insects and disease, animal parasites, prevention of malaria, as applicable to tropical climes will commend themselves at once to one planning a sojourn in this part of the world.

Indeed, in no way, so quickly as by familiarizing one's self with this little work, can the stay-at-home become informed on a topic of such general interest. A. A. H.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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On the So-called Granular Form of the Tubercle Bacillus.—G. BRÜCKNER (*Ztschr. f. klin. Med.*, 1914, lxxx, 360) has taken up the study of the non-acid-fast, so-called granular form of the tubercle bacillus as described by Much. As a result of his study, he concludes that the modified Gram's stain for the demonstration of the Much's granules in the sputum is unreliable for the diagnosis of tuberculosis. This applies not only to the smeared sputum, but also to antiformin preparations. Groups of granules arranged in rod form are to be looked upon as tubercle bacilli in the sputum, but these in the author's experience are found in sputa only when acid-fast tubercle bacilli are demonstrable. The author considers the granules as nothing more than tubercle bacilli demonstrable by the modified Gram's stain. They do not represent a special form of the tubercle bacillus.

An Experimental Study of the Relation of the Ductless Glands to Purin Metabolism.—FLEISCHMANN and SALECKER (*Ztschr. f. klin. Med.*, 1914, lxxx, 456), in attempting to shed light on the still obscure problem of gout, have made an experimental study in the dog of the effect of the glands of internal secretion on purin metabolism. They give extensive protocols of their experiments, only their conclusions can be given here: Nucleinic acid fed to dogs is excreted almost quantitatively. This condition is changed when pituitrin is administered at the same time, resulting in a decrease and retardation of the excretion of allantoin. When pituitrin is injected into an animal which has been placed on a purin-free diet, there frequently occurs a slight increase in the excretion of allantoin with a subsequent drop. In a

fasting dog, however, this increase is missed. Adrenalin, when injected in fairly large doses, produces a marked increase in excretion of allantoin without increase in total nitrogen. The reverse effect is observed after injection of phloridzin; the total N is increased but there is no change in allantoin. In thyroidectomized animals nucleinic acid which is fed is excreted in lessened amount. Likewise under the influence of iodothyrin, there is a diminished excretion of allantoin which coincides with the marked protein destruction. Administration of paraglandol (parathyroid gland substance) has had no certain effect on purin metabolism. Purin bases fed to fasting animals are appareatly partly retained. An excess of fluid causes a marked rise in allantoin excretion.

Studies of the Blood in Variola and Vaccinia.—M. SCHATZMANN (*Ztschr. f. klin. Med.*, 1914, lxxx, 333) has made careful studies of the blood in seven cases of variola, two of which were fatal, and also in vaccinia. In the incubation stage of variola, the author finds a polynuclear leukocytosis. As the eruption begins to appear and as long as it remains papular, the white count is normal or subnormal. With the appearance of the vesicular stage, the white count again increases, leading to a more or less marked leukocytosis, due chiefly to increase in lymphocytes. A relative lymphocytosis persists for weeks. A marked increase of the polynuclear neutrophile cells indicates a complication. During convalescence, the eosinophiles which never completely disappear increase in number. In severe cases Türck's irritation forms, myelocytes and erythroblasts are found. A considerable number of myelocytes and erythroblasts with only a slight leukocytosis is an unfavorable sign. The persistent lymphocytosis is of some value for a retrospective diagnosis in epidemics. During vaccinia, there is a moderate increase of the white count the first day following the inoculation. By the time the local and constitutional symptoms have reached their heighth (seventh to tenth day) the leukocyte count falls, at times to normal. Then there ensues a second rise in count. The primary leukocytosis is a polynuclear, the secondary a lymphocytic. Here, too, usually during the second week, Türck's irritation forms and myelocytes are present in small number for a day or so. Finally, there may be a slight increase in the eosinophiles. There is thus a striking similarity in the leukocyte picture of variola and vaccinia, suggesting their identity.

A Study of Protein Metabolism in Experimental Pancreatic Diabetes.—A. GALAMBOS and B. TAUSZ (*Ztschr. f. klin. Med.*, 1914, lxxx, 381) in a previous communication showed, contrary to the generally accepted view of the time, that hyperaminosuria occurs not exclusively in cases with impaired liver function, but also in cases of disturbance of the internal secretion of the pancreas (diabetes). Indeed, the most extreme grade of hyperaminosuria they encountered (17 per cent.) was in a diabetic with acidosis. In mild cases of diabetes on the other hand, normal values for amino-acids in the urine may be found. In diseases with increased protein catabolism such as cancer, leukemia, most febrile infections, there is a tendency to a more or less marked hyperaminosuria though it is not constant. Their clinical findings, the authors have attempted to reproduce experimentally. They reason

that if hyperaminosuria occurred after complete removal of the pancreas but was absent after ligation of the pancreatic duct, this would practically prove that the determining factor was the internal secretion of the pancreas. The experiments, therefore, were conducted on this basis. Dogs were used. They were placed on a standard diet and the ammonia, total nitrogen and amino-acids of the urine were determined during a control period of three to eight days before the animals were operated upon. The authors found that the results conformed to what they expected. The catabolism of protein to its normal end products requires the internal secretion of the pancreas. An insufficiency of this secretion leads to hyperaminosuria. Pancreatic glycosuria and hyperaminosuria, they look upon as analogous phenomena. Diseases of the liver and acute infections may be accompanied by hyperaminosuria, just as alimentary hyperglycemia or glycosuria may be associated with them. It is possible that both metabolic anomalies have a common cause, and it is quite possible that this is to be sought in a decrease or loss of the internal secretion of the pancreas.

On the Vaccine Treatment of Typhoid Fever.—A. V. KORANYI (*Wien. klin. Wchnschr.*, 1915, xxviii, 85) has recently treated a small series of typhoid fever patients with Ichikawa's vaccine with such good results that he considers a report advisable. The vaccine was prepared after the method of Ichikawa. Ten loopfuls (oese) of typhoid bacilli were added to 10 c.c. of serum from a convalescent, incubated five to six hours, washed and then shaken in 100 c.c. normal salt solution containing 0.3 per cent. phenol. Experiments showed that 0.4 to 0.5 c.c. of this preparation is the proper dose. After establishing this point, the author treated twenty-four cases of typhoid fever with the vaccine. No deaths occurred. Following vaccination, a more or less severe reaction occurred, chill, rapid rise of temperature, followed by a fall almost to normal or even subnormal, with free perspiration. The reaction was very well borne. The further course of the disease may be divided into four groupings: (1) critical fall of temperature with recovery (seven cases); (2) a fall of temperature by short lysis (three cases); (3) marked improvement (seven cases); (4) no appreciable betterment (seven cases). The earlier in the disease the vaccine is given the better appear to be the results. Recurrence may follow abortive cure, but it also yields to vaccination.

Comparative Determination of Blood Sugar by Polarization and Reduction Methods.—C. MAASE and H. TACHAU (*Ztschr. f. klin. Med.*, 1914, lxxxi, 1) report the results of a comparative study of determination of blood sugar by polarization, by copper reduction (Bertrand) and by silver reduction (Tachau). In twelve cases examined, including three of diabetes, the results of the three methods were practically the same, excepting in one case of diabetes where the polariscopic readings were considerably higher than those obtained by the reduction tests. The reason for the difference, the authors were unable to determine. On the whole the polariscope gave results a trifle higher than the reduction methods; Tachau's method usually gave a slightly higher result than Bertrand's. Interesting results are reported after the administration of 100 grams of levulose. As would be expected, the

polariscopic readings were increased, reduction decreased. Using the specific polarization and reduction values for dextrose and levulose, the authors calculate the amount of sugar in the blood. Levulose was highest in a patient with jaundice.

On the Treatment of Delirium Tremens with Veronal.—E. VON DER PORTEN (*Deutsch. med. Wchnschr.*, 1915, xli, 34) warmly recommends veronal in the treatment of delirium tremens. During the years 1910 to 1913, he has treated 382 cases of delirium tremens with veronal; the mortality was 5.49 per cent. The veronal was given dissolved in warm tea. On admission the patient receives 1.0 gm., and one to two hours later a second similar dose is given. If this does not suffice to quiet the patient, another gram is given five hours after the first dose. In very resistant cases a further dose may be required within the first twelve hours.

SURGERY

UNDER THE CHARGE OF

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Typhoid Spine.—CARNETT (*Ann. Surg.*, 1915, lxi, 456) says that over one hundred cases of typhoid spine have been reported since the publication of the first paper by Gibney, in 1889, but less than thirty cases in which Roentgen-ray pictures were taken, and in some of these the roentgenograms were negative. To this list he added three personal cases in which the Roentgen rays disclosed definite bone changes, and says that sufficient evidence has been accumulated to prove definitely that Gibney was correct in his original view that an inflammatory organic lesion does occur in these cases. The cases which only simulate typhoid spine, whether because of neurosis, toxemia, or any other cause, but which do not present organic changes, should henceforth be excluded from the list of true typhoid spine cases. A negative roentgenogram does not disprove the presence of an organic lesion. It has been found that fully 85 per cent. of the cases occur in males, that it is most common between twenty and twenty-five years of age, and occurs as commonly in mild cases of typhoid fever as in severe ones. The vast majority of cases occur in the lumbar spine or in it and the immediately adjacent thoracic and sacral vertebræ. Commonly only two adjacent vertebræ are involved, though, rarely, several may

be: Fraenkel found typhoid bacilli more frequently in the lumbar vertebræ, probably, because of the larger amount of bone marrow in them. The lumbar spine is also normally subject to greater stress and strains than the remainder of the spinal column. Typhoid spine is almost never fatal, hence post-mortem study of recent cases is wanting. The onset of symptoms was usually gradual, but in many was abrupt and acute, occurring in a few cases during the febrile period, most often during convalescence, and quite frequently some weeks or months, in one case four years, after recovery from typhoid fever. The Widal tests, when taken, have been positive. Pain over the spine has been the most constant and positive symptom, as well as usually the first to attract attention. The local pain, however, has sometimes been shadowed by the greater intensity of the referred pains. Local pain is aggravated by movements or jarring of the spine and local tenderness can be elicited and the spine is rigid in all cases, in only three or four cases did suppuration result requiring incision. The Roentgen-ray in the later stages affords the best proof of a local lesion. The great majority of the patients experienced severe or even excruciating radiating pains, especially on movements of the spine. The best form of treatment is to place the spine at as near absolute rest as possible. This may be accomplished by either plaster-of-Paris cast, spinal brace, or by continuous traction from head and feet. Pain often has ceased abruptly after fixation of the spine. Excessive pain can be relieved by the local application of heat, by aspirin or sedatives, but often opiates will be needed. Elimination should be pushed to combat the toxemia. In prolonged cases vaccines may be of service.

Tuberculosis of the Knee-joint in Childhood.—SEVER and FISKE (*Amer. Jour. Orthop. Surg.*, 1915, xii, 597) studied a series of 638 cases admitted to the Orthopedic Department of the Children's Hospital, in Boston, from 1880 to 1910. The object of this investigation has been to furnish some general statistics, based on this large number of cases, to report as far as possible the varying symptoms, pathology, etc., that were met with, and to record the results of treatment under the different methods employed, as they applied to different conditions and groups. It was found that the males predominate and the right and left knees are equally affected. Trauma occurs in 30 per cent., tuberculous family history in 13.5 per cent., involvement of other joints 11.3 per cent., in order of frequency the hip, spine, ankle, elbow and wrist. Predominant symptoms occur in the following order of frequency: swelling, limitation of motion, flexion, heat, pain, subluxation, abscess, sinus, fluid, knock-knee, and outward rotation. Abscess occurred in 27 per cent. of all cases. Osteal involvement predominates in children, but synovial disease is found frequently with it. Disease of tibia alone is rare, involvement of tibia and femur together is commonest, of femur alone is next. Bony enlargement is commonest in femur alone, and in the internal condyle. Treatment was by traction, plaster, splint, and operation. Thirty-five per cent. were operated upon, the relative frequency of the operations being forcible correction, incision and drainage, osteotomy, tenotomy, excision, arthrotomy, aspiration and amputation. The first four types of operation had to be repeated in many cases. The average duration of treatment was 4.9 years, cases

not operated on averaging 4.2 years, those operated averaging 5.8 years. The results of treatment of 251 of these cases of three years or more duration under treatment show that about 65 per cent. had satisfactory results, 35 per cent. unsatisfactory, the oldest cases showing the best results, healing and ankylosis increasing with duration of the lesion. Although the cases operated on undoubtedly represent the severest types, it is significant that much better results were obtained in the non-operated cases, one-quarter of the latter as compared with one-half of the former having undesirable results. Forcible correction and excision were the only operations in which more favorable than unfavorable results were recorded. Outside of the few probably favorable cases which received splint treatment only, the best results in the non-operated cases were obtained by the combined splint and plaster treatment, if the healed cases be taken as a criterion, otherwise there is little choice in the method of treatment. The results of those cases which were in the worst condition at admission, as represented by the groups which were put in traction, or had abscesses, compare unfavorably with the general average, showing a predominance of unsatisfactory results and many unhealed cases. The results of those cases of abscesses not operated are, however, far better than those which were opened.

Tuberculosis of the Hip, an Analysis of Twenty-five Selected Cases.—Allison (*Amer. Jour. Orthop. Surg.*, 1915, xii, 623) says that these cases were treated at the Saint Louis Children's Hospital within the last four years, and have gone on to recovery in that they have ceased to have symptoms and have weight-bearing joints. The analysis of these cases is intended to demonstrate the value of the Bradford traction-abduction splint in the routine treatment in the ambulatory stage of hip-disease. In view of the fact that the extent of the ankylosing process is dependent upon the intensity of the disease process and the amount of destruction of the joint cartilage, it is very essential to protect the hip-joint both from weight and from motion in the acute stages of the disease, and during the convalescent stage traction properly applied is a most important element in successful treatment. Allison is not of the opinion that an ankylosed joint is the best result that can be obtained in hip-disease, and he feels that what Lorenz calls the "weight-bearing therapy" is an incomplete and careless manner of treatment. He has gained from the cases studied the following facts: The average shortening where plaster-of-Paris spicas were used was 1.45 inches; where the Bradford traction-abduction splint was used it was 0.56 of an inch. Where plaster-of-Paris spicas were used the average atrophy of the thigh was 1.47 inches, and of the calf $\frac{1}{2}$ inch; where the Bradford traction-abduction splint was used the average atrophy of the thigh was 1.27 inches and of the calf 0.76 of an inch. The use of traction, therefore, does not materially increase the amount of atrophy. Motion was preserved to all the hip-joints treated with traction-abduction splint and was lost in 60 per cent. of the cases treated with plaster-of-Paris spicas. Abscesses have occurred in 33 per cent. of the cases treated with plaster-of-Paris spicas, and in 40 per cent. of the cases treated with traction-abduction splints. Of the cases treated with plaster-of-Paris spicas there were six cases that developed

complete bony ankylosis. In five cases it was necessary to do an osteotomy of the femur in order to correct adduction and flexion deformity. Two of the cases recovered with free motion in all directions; two recovered with motion through 45 degrees in flexion. Of the cases treated with Bradford traction-abduction splint no case resulted in bony ankylosis, and in no case was it necessary to correct deformity by osteotomy. All the hips were held in position of abduction.

THERAPEUTICS

UNDER THE CHARGE OF

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An Experimental Study of Methods of Prophylactic Immunization Against Typhoid Fever.—GAY and CLAYPOLE (*Arch. Int. Med.*, 1914, xiv, 67) review the history of the development of artificial immunization against the typhoid bacillus in animals and human beings and discuss some of the many preparations of the typhoid bacillus used for this purpose. Particular attention is drawn to the reputed advantages of living sensitized typhoid vaccine (Besredka) as opposed to other types of vaccine. The many vaccinns that are still being advocated indicate that the best vaccine has not yet been found and that the best method of proving which is the best vaccine has not yet been determined. Sensitized cultures of the typhoid bacillus, whether whole or as sediment, produce little or no reaction in human beings with the possible exception of those who have previously suffered from typhoid or those who have been immunized. By comparing their results with those of certain other observers, the authors conclude that a considerable degree of reaction, both local and general, is avoided by the use of these sensitized cultures, which possess the further advantage, so far as their experimental work can determine, of producing a more durable type of immunity. Gay and Claypole recommend vaccination at short intervals (two days) in human beings, which is rendered quite possible with the mild vaccine they employ, and is evidenced from animal experimentation, as giving rise to less toxic effect and to fully as durable an immunity as vaccination at longer intervals. This type of vaccination has the further advantage of completing the prophylactic treatment of three injections within a week. They further believe that a polyvalent vaccine derived from strains of the typhoid bacillus isolated in the vicinity of patients who are to be treated is advantageous, judging largely from the work of other observers. A further advantage in the use of sensitized cultures is that a polyvalent vaccine, no matter how recently the strains may have been isolated, is also almost entirely free from untoward effect. They recommend for prophylactic immunization against typhoid, three injections of the

sediment of a dried, ground, sensitized culture of several local strains of the typhoid bacillus mixed together, given at two-day intervals and in a dosage of $\frac{3}{32}$ mg. of the original dried culture, which corresponds, as has been determined, to a dosage of approximately 750 million living typhoid bacilli. Gay and Claypole state that their experimental and clinical results as well as the work of many other investigators lead them to believe that the agglutinating power of the serum is by no means indicative of the degree of protection afforded against infection with the typhoid bacillus. They believe that the skin test with the typhoidin solution is of far more prognostic value. They state that persons immunized with various types of typhoid vaccines react in the majority of cases for about two years and then become more frequently negative. The authors regard a negative skin test after vaccination as an indication for revaccination.

A Clinical and Bacteriological Study of Hexamethylenamin as a Urinary Antiseptic.—Levy and Strauss (*Arch. Int. Med.*, 1914, xiv, 730), in an endeavor to ascertain the value of hexamethylenamin as a urinary antiseptic, examined the urines from 91 patients receiving this drug. Most of the urines were examined twice and some of them as many as six times. The 91 cases may be divided as follows: surgical 42, medical 32, and genito-urinary 17. The urines of all of the 91 patients gave a test for formaldehyd varying from 1 to 20,000 to 1 to 5000. The urines from 72 patients showed the presence of formaldehyd in the strength of 1 to 10,000. They conclude that in almost all cases hexamethylenamin is excreted into the bladder unaltered and thin, under the influence of the acid in the urine and the warmth of the body, is broken down into formaldehyde. They believe that in those cases in which formaldehyd is liberated in the kidneys it is probably due to the higher than normal acidity of the urine in the kidneys. These are undoubtedly the cases that develop a hematuria or albuminuria. The authors tried the effect of hexamethylenamin in a 10 per cent. neutral solution and found that it had neither bactericidal or inhibitory influences upon bacterial growth. They found that formaldehyd to be of value as a urinary antiseptic must be liberated in strengths varying from 1 to 15,000 to 1 to 5000 depending on the organism the growth of which is to be inhibited. To be of bacteridical value it must be liberated in strengths from 1 to 5000 to 1 to 1000, also depending on the organism. They determined the concentration of formaldehyd in the urines examined by the Rimini method which gives only an approximate estimation. By this method they never demonstrated formaldehyd in a concentration greater than 1 to 5000. Hence they believe it reasonable to assume that formaldehyd is never present in urine in solution strong enough to destroy any organism except the bacillus typhosus. However, it may exert an inhibitory action on other organisms. They found that a high acidity is necessary for the destruction or inhibition of organisms other than the typhoid bacillus. This high acidity in combination with the formaldehyd may produce injury to the kidney tissue. The final conclusion of the authors is that hexamethylenamin appears most efficacious as a prophylactic during the course of typhoid fever for the prevention of pyelitis or cystitis. Its successful use in this connection has been demonstrated both clinically and bacteriologically.

Mouth Infection as a Source of Systemic Disease.—Billings (*Jour. Amer. Med. Assoc.*, 1914, xliii, 2024) confines his remarks to alveolar infection of the jaws as related to systemic disease. Chronic arthritis has been especially studied, and in order to make a proper diagnosis of the cause of the disease radiographic films of the jaw must be made. Alveolar infection and root abscesses may be primary and due to unhygienic conditions of the mouth, but Billings believes that irrational dentistry—teeth with infected pulp, crowned or improperly filled—prolongs and intensifies the infection. The chief systemic diseases induced by such infection are malignant endocarditis, chronic arthritis, and myositis. Cultures were made from the infected alveoli and tooth sockets. The dominant organisms found belong to the streptococccus-pneumococcus group. In addition staphylococci, a fusiform bacillus, the Bacillus aërogenes capsulatus, and various saprophytic organisms were found. In five patients suffering from Hodgkin's disease, an alveolar abscess has culturally yielded the diphtheroid bacillus, which is found in the enlarged lymph nodes in that disease. After removal of the source of the infection the attempt should be made to increase the defences of the body against the systemic infection. Autogenous vaccines may be used to assist the body in overcoming the systemic infection but should be considered only as aids in the treatment. General hygienic and tonic measures to increase the resistance of the patient are essential. The treatment of chronic joint affections is long and tedious and must be supplemented by graduated passive and active exercise and other measures to improve the local circulation in the joints involved.

The Vaccine Treatment of Typhoid.—V. Koranyi (*Wien. klin. Wchnschr.*, 1915, xxviii, 85) reports a series of cases of typhoid which were treated by Schikawa's serum. This serum is, briefly, a mixture of typhoid bacilli and serum from typhoid convalescents. The details of the preparation of the serum are not given in this article. In all, 24 cases were treated with no mortality. A considerable reaction, as a rule, followed the injection of the serum usually in the form of chills and a rise of temperature followed by a sudden fall. The fall in temperature was so marked that at times the temperature became subnormal. He divides the cases treated into four groups: First, those that make an unevently recovery with, as a rule, a critical fall in temperature. The second group includes those cases in which the temperature rises moderately after the injection of serum and then comes down by lysis in a few days. The third group comprises those cases in which after a sharp rise in temperature there is a sudden and decided improvement in the clinical symptoms. The fourth group includes those cases that did not seem to be influenced favorably or otherwise by the injection of the vaccine. V. Koranyi says that it cannot be definitely determined whether a revaccination would not help after the primary vaccination failed. He believes that some cases of typhoid fever can be aborted by means of this vaccine. The first week of the disease is the best time for successful treatment. He adds that cases that have been aborted and subsequently recur usually respond the second time to the abortive treatment.

The Present Status of the Crotalin Treatment of Epilepsy.—Thom (*Boston Med. and Surg. Jour.*, 1914, clxxi, 933) opposes the foundation upon which the crotalin treatment of epilepsy is based; namely, that epileptic convulsions are induced by increased coagulability of the blood and that the good effects obtained by crotalin therapy is due to its action in lessening the coagulability. Thom tested the coagulability of the blood in 203 epileptic patients free from any clinical evidence of organic brain lesions. Blood was taken for this purpose before, during, and after convulsions; 92 per cent. of these cases fell within normal limits; 5.5 per cent. was less than the minimum limit, and 2.5 per cent. over the maximum limit. Thom was convinced there was no relation between the coagulation time of the blood and convulsions in epileptics. Fourteen cases of idiopathic epilepsy were started on crotalin with the intention of continuing for three months. On three of these patients it was necessary to suspend treatment; in the first case because of the development of hysteric attacks; in the second the convulsions were so markedly increased in frequency and severity that at the patient's request treatment ceased; the third case exhibited such violent local and systemic reactions that Thom did not feel justified in continuing the injections. Of the remaining eleven cases which were kept on treatment for the three months, six became worse, that is, the convulsions were either increased in frequency and severity or some unusual mental disturbance made itself manifest; four showed no change whatsoever; and one, a typical case of hystero-epilepsy, showed improvement, undoubtedly the psychological effect of the administration rather than the drug being the cause. Thom collected a total of fifty-eight cases from Pennsylvania, Virginia, and Michigan. Six, or less than 10 per cent., showed improvement; twenty, or more than 35 per cent., became worse, and three died while treatment was being carried out. The remaining twenty-nine cases were apparently unaffected by the drug. Thom mentions among other disadvantages of applying the crotalin treatment that the remedy is frequently contaminated by anaërobic organisms and that it is impossible to obtain a standardized dosage, as pointed out by Noguchi who found that crotalin lost from 25 to 50 per cent. of its strength in the process of drying.

The Treatment of Tetanus.—Siemon (*Münch. med. Wchnschr.*, 1914, lxi, 2322) reports 26 cases of tetanus, the first 10 of which were treated with serum alone and only one recovered. Since then magnesium sulphate was used and in some cases without serum and in others combined with the serum treatment. Of 11 cases treated with serum, magnesium sulphate, and other symptomatic remedies not one was lost. He does not speak definitely of the five other cases, which may still be under treatment. He believes that the remarkable change in the mortality must have been due, in part at least, to the symptomatic use of magnesium sulphate. Narcotics were used very sparingly in the treatment of those given magnesium sulphate; a small dose of chloral was given in the evening to secure sleep, In the wounded coming under Siemon's observation the number of cases of tetanus among the Germans was about five times the number among the French. The author suggests that the higher incidence of tetanus in the German soldiers must be due to some special factor as yet unexplained.

PEDIATRICS

UNDER THE CHARGE OF

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Patent Ductus Arteriosus.—E. W. HALL (*Archives Middlesex Hospital* xxxi, 39) reports three cases of patent ductus arteriosus. The first child, aged two weeks, was attacked suddenly by cyanosis and cessation of breathing. On admission to hospital it appeared healthy. There was nothing to suggest organic disease, and no physical signs of any heart lesion were present. The child had several subsequent attacks, succumbing to one of them. Respiration ceased and cyanosis developed rapidly. The heart, however, continued to beat regularly and the pulse could be felt at the wrist. The heart sounds became inaudible toward the end of the attacks. At autopsy the only lesion found was a patent ductus arteriosus, which was large enough to allow the passage of a large probe. The second child, aged two weeks, had similar attacks. No murmurs were heard over the cardiac area, but there were signs of bronchitis in the lungs. The child died during an attack, and the patent ductus arteriosus was the only abnormality found. The third child, aged three weeks, had a similar history and had typical attacks of cyanosis with complete inhibition of respiration, requiring artificial respiration for twenty minutes and oxygen and brandy to revive it. Autopsy again showed only patent ductus arteriosus. Most cases are reported as occurring in combination with other forms of congenital heart lesions, especially pulmonary stenosis. The cyanosis is probably due to a deficient aëration of the blood. The systolic murmur heard over the cardiac area, as described in the text-books, was absent in these cases. There was also no sign of obstruction during the intervals of the attack.

Cerebellar Abscess in a Child.—ASHBY (*Brit. Jour. Child. Dis.*, 1915, xii, 105) reports a case of cerebellar abscess in a child aged 4 years; in which the only symptoms were continued headache and listlessness and continued posture of lying on the right side. There was a slight bronchitis and the pulse was slow and irregular. The temperature was normal throughout and the cerebrospinal fluid was not under pressure, was clear, and normal except for a slight excess of lymphocytes and polymorphonuclears. The urine was normal and there had never been any discharge from the ears. Optic neuritis was present and became slowly worse but the pupillary reactions were normal. She was in hospital five weeks and lay in her usual position on the right side maintaining her listless attitude. For the last three weeks she vomited on an average of two or three times a day. After five weeks she had a right-sided convulsion and died. No diagnosis had been made except an improbable one of tuberculous meningitis. On autopsy a large abscess was found in the substance of the right cerebellum. The pus was creamy and contained pneumococci. The

origin of the abscess is not discernible as the ears were normal. The slight bronchitis may have been the starting point. The few localizing symptoms during life were the persistent lying on the right side and the right-sided convulsion. There was no nystagmus or tendency to fall to one side more than another.

The Oculo-cardiac Reflex.—Gunson (*Brit. Jour. Child. Dis.*, 1915, xii, 97) gives the history of the investigations into the oculo-cardiac reflex and his observations of it in observations with the polygraph in cases of diphtheria and scarlet fever in children under twelve years of age. Observations made by Mackenzie on cases of acute rheumatism were similar to those made by Gunson. This reflex consists of a reflex change in the rate of the heart and often in the rhythm following ocular compression. The path of the reflex is supposed to be along the fifth cranial nerve, medulla and vagus or sometimes the sympathetic. It produces the same cardiac changes as vagus pressure in the neck. When there is no slowing, or actual quickening of the pulse the result is negative. The reflex is positive in normal persons. It is positive in 92 per cent. of children convalescent from diphtheria and scarlet fever. In 8 per cent. the reflex is negative. These are highly nervous cases. In cases of so-called cardiac paralysis the reflex is negative. In cases that recovered the reflex became positive when the heart returned to normal. Among the cardiac results obtained in positive reflexes were, slowing of the whole pulse with stoppage of the heart in some cases as long as four seconds; production of premature contractions, reduction of the a-c interval and in diphtheria cases only complete dissociation of auricles and ventricles. The oculo-cardiac reflex is apparently of no diagnostic importance unless in confirming the nervous origin of postfebrile bradycardias. Gunson claims it does not differentiate cardiac failure from myocardial lesions from that due to nervous lesions since this would presume the independence of the muscular and nervous functions of the heart.

Rupture of the Heart in a Child.—Anderson (*Lancet*, 1915, clxxxviii, 647) reports a case of rupture of the heart in a girl five years old and apparently in fair if not good health. A hematoma was found in the left ventricular wall. The cavity was filled with blood and it had ruptured externally into the pericardium. There was an extensive rupture across the inner portion of the posterior wall of the chamber and the torn area almost encircled the ventricle. There was a stenosis of the lumen of both coronary arteries and the left one was obliterated at the seat of rupture. The lymphoid tissue throughout the body was increased in amount and the liver was large and waxy in appearance. Microscopically there was shown increased fibroid tissue through the heart muscle and liver. There was thickening of the vessel walls of the heart with frequent thrombosis. While the explanation of this condition may be that of thrombosis and abnormal development of the coronary arteries, or to necrosis of the heart wall from infarction, still the probable cause, primarily, was a syphilitic endarteritis. Inherited syphilis is a frequent cause of congenital heart disease. The work of Warthin has shown the heart to be a favorite lodging place for the Spirocheta pallida, even when they were not demonstrable

everywhere else in the body and that a large percentage of congenital cardiac conditions are due to this cause and lead subsequently to arteriosclerosis. In the present case a few spirochetæ were found in the heart muscle, and many in the kidney, so that with the evidences of syphilitic processes in other parts of the body the cardiac findings can be interpreted as congenital syphilitic disease.

OBSTETRICS

UNDER THE CHARGE OF

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Icterus in the Newborn as an Infectious Disease.—PFÄLTZER (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reviews the reports of cases by Schmorl, Beneke, and Esch, and adds a case under his observation in the clinic at Halle. The child was the fourth of a healthy mother, whose second child was stillborn, the two others living and vigorous. There was nothing abnormal about the pregnancy, labor was spontaneous, the child was born living and cried vigorously. The effort was made to have the child nurse, and as the mother's supply was insufficient the bottle was given, but was not well taken. The child was finally fed with a spoon. On the second day after birth well-marked icterus developed. The child was apathetic and moved but little, the temperature rose at evening to 103°, and at the end of the night the child died. At autopsy, the color of the skin was both icteric and cyanotic. The toes and fingers were drawn in convulsively. The stump of umbilical cord was dry, but the tissues about the umbilicus were infiltrated. Both legs were slightly edematous. There was ecchemosis of the conjunctiva. The ears, nose and mouth showed nothing abnormal. The abdomen was soft and not especially large. The fatty tissue was not in excess, the muscular tissue dry, pale, and icteric. In the region of the umbilicus on the inner aspect there was edema; no suppuration was present, and the vein and arteries were normal. The situation of the abdominal organs was normal, and in the region of the head and face there was bleeding into the substance of both temporal muscles. In the longitudinal sinus there was dark fluid blood but none beneath the dura. At the base of the brain there was a peculiar grayish-yellow color, which became deeper in some portions. There was no especially jaundiced color in the convolution of the brain or the medulla, but some other portions were markedly jaundiced. This was especially true in the region of the optic thalamus. The same was true of the medulla oblongata. The hypophysis in its nerve fibers was a deep yellow in color. In the pericardium there was bile-stained fluid. About the tongue the tissues were jaundiced, and there were patches of necrosis on the tongue, esophagus and larynx, deeply colored. The yellow exudate simulated somewhat a diphtheritic

membrane. The spleen was much enlarged, dry and dark red. The stomach was dilated and contained colorless mucus. The mucous membrane of the stomach was dark red and showed small portions stained deep yellow. This was also true in the duodenum. The mucous membrane of the bowel was somewhat thickened and dry, the liver not markedly jaundiced, the gall-bladder full of bile, the suprarenal bodies very large and grayish in color, the kidneys full of uric acid infarcts, and the urinary bladder stained a deep yellow. There was nothing of especial interest in the muscles. Microscopic examination of portions of the brain and nervous system showed the intense yellow staining of nuclei, which has given to this disease the name of nuclear jaundice, or in German, "kern icterus." Bacteriological examination of the blood was negative, although crystals of bilirubin were present. Bacilli-like staphylococci were found in great abundance in mucus taken from the esophagus. Blood from the heart, spleen and also the bile, was sterile. From the liver was obtained the Bacillus coli communis, and this germ was found in the region of the umbilicus, and also in some of the muscles. In searching for the point at which the infection gained entrance to the body, the esophagus was thought to be the point of infection. The diagnosis of nuclear jaundice, or kern icterus, with diffuse myositis resulting from infection by the B. coli communis, and staphylococci, was made. The three points of clinical interest which seem to go together, are the presence of the B. coli communis, multiple lesions in the muscles, and the changes in the nuclei in the tissues of the nervous system. As regards diagnosis during life, one must observe the presence of jaundice, and when to this is added convulsions or convulsive movements of the muscles, if the patient be an infant, the diagnosis may be provisionally made.

Fibroids of the Uterus and Twin Pregnancy.—Montuoro (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reports the case of a multipara in the third month of pregnancy with interstitial fibroids in the uterus. It was determined not to interfere, with the hope that in some way spontaneous birth might occur. Two weeks after the patient was first seen, at the middle of the third month she had severe pain and hemorrhage, and an abortion with twin ova. Two months later hysterectomy was performed. The writer also reports the case of a multipara, aged forty-two years, who suffered from metrorrhagia and menorrhagia, for which a curetting and amputation of the stump was done. It was found that the patient had in addition a fibroid tumor of the uterus. Some years afterward she became pregnant and the fibroid tumor had considerably increased in size. A physician who was consulted attempted to produce abortion, which resulted in profuse hemorrhage which threatened the patient's life. From this she gradually recovered, and afterward became again pregnant with twins. This pregnancy terminated in sudden abortion at about the third month. After this second abortion the fibroid growth increased enormously in size, and hysterectomy was performed. The patient made a tedious recovery from the operation, having had a thrombus in a vessel in the left lower extremity. The third case reported was that of a primipara, aged thirty-one years, married five months, and pregnant about three months. She had suffered much from abdominal pain, with edema of the lower extremities and interference with the functions of

the bladder. On examination, the urine contained 2 per cent of albumin. On palpating the abdomen a hard and painful tumor was found in the region of the uterus, the genital organs were bluish in color, and the cervix drawn toward the left side. The characteristic conditions of early pregnancy in the pelvis were present. A diagnosis of fibroid tumor and early pregnancy could readily be made out. The uterus was drawn considerably toward the left, and the effort was made to bring it into the direct axis of the pelvis. Abdominal section was accordingly performed and the uterus found to be within one of the broad ligaments. It was possible, however, to sever the broad ligament tissues to bring the uterus up, and perform hysterectomy. During the operation the amniotic sac was opened, and through this opening a foot of the fetus was observed. The removal of the uterus was accomplished without difficulty and the abdomen closed without drainage. When the uterus which had been removed, was examined, it was found that uterine contractions had expelled a fetus. On the following day a second fetus was also expelled. The mother made a good recovery. This case is reported to illustrate the fact that patients with fibroid tumors of any size can rarely go to full term in pregnancy. A collection of 15 cases is added, with the salient points of each. If one examines the material, from the standpoint of the statistics, we find that pregnancy proceeded normally in 28 per cent.; that abortion happened in 16 per cent.; and that surgical interference was practised in 56 per cent. The majority of operators interfere surgically so soon as it is evident that the tumor is of any size and likely to obstruct labor.

Eclampsia and Sugar in the Blood.—Widén (*Monatschr. f. Geburts. u. Gynäk.*, 1915, Band xli, Heft 2) describes his investigations to determine the presence of sugar in the blood in cases of eclampsia. There is an excess of sugar in the blood during eclampsia which appears intermittently. Concerning the origin of this sugar nothing positively is known. The intoxication theory is probably the most rational. Albuminuria is not a criterion of renal intoxication, and in these cases the quantity of blood sugar varies greatly. The blood of the fetus shows no increase in blood sugar corresponding to that in the mother.

The Treatment of Placenta Previa.—Stratz (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) quotes the statistics of placenta previa as reported by different leading obstetricians of Holland, as 881 cases with a maternal mortality of 7 per cent., a fetal mortality of 43 per cent. These statistics pertain to the year 1914. In comparison with these are 236 cases treated by combined version, with a maternal mortality of 2.7 per cent., a fetal mortality of 68 per cent. His experience in the clinic at The Hague leads him to rely upon the following methods, which are available for the general practitioner in most cases: When the bleeding is not severe the patient should be put at absolute rest and narcotics given. The writer states most emphatically that in no case should the vaginal tampon be employed. Where the bleeding is severe, combined version should be performed, and the patient kept under control while the fetus is very slowly and carefully drawn into the cervix. Efforts at extraction should then cease, and the obstetrician should wait until the mother has expelled the child up to

the shoulders. Delivery should not be hurried. The final extraction of the child should be done very gradually and with great care. No effort should be made to save the life of the child at the risk of the mother; and the two procedures to be avoided, in his experience, are the use of the tampon and the immediate and rapid extraction of the fetus. For cases taken to hospital, where the cervix is not dilated, delivery by Cesarean section will be advantageous.

The Cause of the High Transverse Position of the Fetal Head, Complicating Labor.—MARTIUS (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) has studied the cases observed in the clinic at Bonn, and reports in detail illustrative cases, in some of which the successful termination of labor was brought about through the use of the Mercurio-Walcher position. In these cases the fetal head was turned transversely across the pelvic brim, and delay in labor resulted from this circumstance. In some the occiput rotated into the hollow of the sacrum while labor proceeded, while in others brow presentation developed. In seeking the causes for this condition, one must remember that the fetal back may turn in any direction during labor; on the other hand, for spontaneous birth to proceed, the head must enter the pelvis in definite relation to the pelvic diameters. These cases are observed where the contour of the pelvic brim may be described as that of a long oval, and where the fetal head also has much of this shape; also where the forces which usually produce rotation as the head passes down into the pelvis fail, as where the pelvis is completely round in shape, or the head is nearly a perfect sphere, or when the head is considerably smaller in proportion than the pelvis. The same condition pertains in cases where the head turns transversely at the brim of a normal pelvis, and the forces of rotation are abnormal; or when in flat pelvis the shape of the head, or the shape of the pelvis, prevents normal rotation. In treating this condition, the great majority of cases terminate spontaneously, in the proportion of 6 to 5, and hence the obstetrician must wait until there is no great disproportion as long as possible before interfering. External manipulation is also useless where the pelvis is contracted in the brim, or where the pelvis is almost completely round in shape. In flat pelvis, if strong version be present, normal mechanism of labor may be expected. The Mercurio-Walcher position is especially useful where there is a tendency to brow presentation, or where the greater portion of the head enters the pelvis at one side of the promontory of the sacrum. This position is the most valuable and simple expedient which we have in the treatment of these cases.

The Cause of Icterus Neonatorum.—HEYNEMANN (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reviews the various theories advanced regarding the causation of icterus in the newborn. In Veit's clinic in Halle he has examined the available material and finds the primary and essential cause to be deficient functional activity in the liver cells in the first days of infantile life. The circumstances which tend to produce this condition are congestion of the liver and unusually rapid disintegration of the red blood cells. The cause of the latter is not clearly known. It seems probable that one must refer it to increased activity in some of the nuclei of the liver cells.

GYNECOLOGY

UNDER THE CHARGE OF

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A Rare Type of Bladder Ulcer in Women.—HUNNER (*Bost. Med. and Surg. Jour.*, 1915, clxxii, 660) reports eight cases of an unusual type of ulcer which he has encountered in women; these ulcers being characterized chiefly by their location, long duration, and resistance to all ordinary methods of treatment. His patients averaged thirty-eight years of age, while the average duration of their symptoms was no less than seventeen years. No etiologic factor could be discovered in any of the histories; three of the patients were single; the others were married and had borne children, but the occurrence of the vesical lesions seemed to have no relation to pregnancy. The ulcers, usually single, but occasionally multiple, were all located in the vertex, or free portion of the bladder, differing in this respect from the simple, solitary ulcer of Fenwick, which is found on the base, or fixed portion. In the cystoscope the ulcers appeared superficial, the granulation surface being on the same general level with the surrounding mucosa, but at operation the inflammatory process was often found to extend through the entire bladder wall, involving even the peritoneum. No deposit of urinary salts was ever seen on the ulcers. The urine in all cases was practically normal; one patient had noticed a little blood at times, but even in her urine only a very few red cells and leukocytes could be found by careful examination. All these patients had in addition to the bladder lesions a granular urethritis, with tenderness and scar tissue contraction, requiring thorough cocainization and very careful manipulation in order to perform a satisfactory cystoscopy. Hunner suggests that possibly the ulceration of the bladder and the inflammatory condition of the urethra may have some common cause, or it may be that the frequency of micturition and straining bring about a hypertrophy and hypersensitiveness of the sphincter region. The cystoscopic picture in these cases cannot be considered in any way characteristic, being merely that of any form of ulcerative condition; the diagnosis depends, therefore, on the resistance of the ulcers to all ordinary forms of treatment. The difficulty of establishing a correct diagnosis is illustrated, Hunner says, by the fact that four of the eight patients had been subjected to operations on other organs in an effort to relieve symptoms caused by the bladder condition. He advocates actual excision of the ulcerated area, after it has been definitely shown that other measures are of no avail. In five of his cases, this was carried out, with complete cure in all but one, in which it is probable that the excision was not sufficiently extensive. Of the other three cases, one has been under treatment for six years, with apparent healing on two or three occasions; the other two have been under treatment for a few months, with but very indifferent results. The operation is done through a suprapubic, extraperitoneal incision, the bladder being distended with sterile fluid or air. The line of excision should

be well outside of the area of inflammation, and the edematous zone which often surrounds it, and should extend through the entire thickness of the bladder wall. The opening thus formed is immediately closed, leaving, however, a small space through which a mushroom catheter is introduced. Through this the bladder is daily washed out with silver nitrate, starting at 1 to 10,000, and gradually increasing in strength, until all traces of infection are eliminated. After removing the catheter, somewhere from the tenth to fourteenth day, the irrigations may be continued through the urethra.

Nerve Cells in the Ovary.—The study of nerve distribution in the ovary has always been beset with many difficulties, and but few satisfactory investigations have been carried out in this field. It is, however, an exceedingly interesting and important one, especially in view of the considerable role that is now being ascribed to the ovary as one of the links in the complex chain of ductless glands, whose secretions are believed to have a more or less active influence upon many of the bodily functions. In this connection, the question as to whether or not actual ganglionic elements exist in the ovary becomes of considerable interest. In discussing in this department a few months ago, Wallart's extensive investigations of the nerve supply of the ovarian substance, it was pointed out that considerable uncertainty has existed as to the presence of true ganglion cells; Wallart himself found structures which he thought must represent such cells, but could not be sure. In a still more recent publication, however, BRILL (*Arch. f. mikr. Anat.*, 1915, lxxxvi, 338) states very definitely that he has been able to demonstrate ganglion cells in ovaries of rabbits and mice, and the excellent illustrations accompanying his article seem to bear out this contention. Brill has carried out his investigations by means of the silver impregnation method of Cajal; he at first attempted to work with human ovaries, but gave these up for those of the animals mentioned above because of the greater ease of securing fresh material, and also because in rodents the internal secretory tissue of the ovary reaches a higher development, and persists longer than in man. The ganglion cells are found, says the author, in compact groups along the course of the nerve fibres, just after these have entered the ovary at the hilus; they are surrounded by a dense network of fibres, and are for the most part multipolar, with several broad-based, branching dendrits. The cell bodies are filled with a delicate network of neurofibrillæ, which converge at the exit of the axis cylinder, into which they can be followed for some distance. From the ganglion cells innumerable delicate nerves pass off to all portions of the organ, especially the follicle system, bloodvessels, and surface epithelium. In addition to the true ganglion cells, Brill found in close relation with them numerous chromaffin cells; these are slightly smaller than the ganglion cells, and do not obtain the network of neurofibrillæ. In conclusion, he states that "this vegetative nervous system of the ovary fulfils every requirement which would be demanded by the secretory function of the organ, without, however, showing any particular relation to the vasomotor innervation."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Perirenal Apoplexy and Sclerosis.—As early as 1841 WILLIS described a disease of the perirenal tissues in which multiple spontaneous hemorrhages and fibroses were the chief lesions. Since then, others have made similar observations and at present some 34 cases have been reported. The pathogenesis is not clear, and LEHNERT (*Frank. Zeit. f. Path.*, 1914, xv, 268) has added another study with the suggestion as to the causative factor. The disease occurred in a man of 62 who had suffered recurrent attacks of rheumatism. Chronic valvular disease was present in the heart, while the kidneys were in a state of advanced interstitial nephritis. Associated with these, there was an unusual development of perirenal fat, throughout which many islands of hemorrhage were found. Evidence of former hemorrhage was also present while grades of inflammation could be demonstrated. It appeared that the individual had suffered repeated attacks of perirenal hemorrhages and repair. There was no evidence that the immediate lesions within the kidney had any association with blood extravasations about the capsule, nor were there any lesions in the adrenals to indicate their association in the process. It would seem that the factors bringing about the renal inflammation were also active in producing a perinephritis. The author believes that much of the hemorrhage was the result of mechanical trauma. That, however, such hemorrhage may be directly associated with the perinephritis is indicated in the report of cases in which there was not only hemorrhage in the perirenal tissues but also in the muscles and other organs.

Experimental Polyneuritis in Birds and Its Relation to Beriberi in Man.—TASAWA (*Ztschr. f. exper. Path. u. Therap.*, 1915, xvii, 27) repeated the experiments of Eijkman and others in reproducing paresis in birds by the feeding of polished rice and grain products. Others have concluded that the polyneuritis gallinarum so obtained was identical with beriberi in man. Some 200 fowl and 120 pigeons were used in these experiments. He found that when birds were fed upon polished rice and water only they suffered great emaciation and nervous debility. Motor weakness developed in about twenty days and progressed until the animals were unable to control any of the voluntary

muscles. Marked degeneration of the motor nerves was demonstrated. In other instances the conditions appeared to arise through a central nervous disturbance rather than peripheral. These cases proved quite different from true beriberi. During the progress of the condition contractures and even convulsive seizures of isolated muscles were observed. The author found that when the feeding with polished rice was accompanied with other foods in moderate quantity the emaciation and anemia could be prevented but the polyneuritis would nevertheless appear. Naturally with the proper quantitative feeding these lesions may be prevented. He found that a similar neuritis can be developed by feeding cane sugar, white flour, white bread or boiled fish. The severity and character of the disease differs but very little from those induced by rice. The subcutaneous injection of rice bran was found to moderate as well as to prevent the disease. It would appear that the disease is the result of metabolic disturbances rather than an intoxication resulting from abnormal fermentation in the gastro-intestinal canal. Up to the present satisfactory results have not been obtained in experimentally producing the disease in mammalia. The results, however, obtained in birds are pathologically so similar to the muscle and nerve degenerations found in beriberi in man that the author believes conclusions can be drawn from these experiments. In animals as well as man there is an individual predisposition which permits of the development of sporadic cases among groups on a common diet.

Experimental Studies on Extirpation of Lung.—KAWAMURA (*Deutsch. Ztschr. f. Chir.*, 1914, 131, H. iii) found that dogs in which one lung has been completely removed, survive the operation and show no ill effects subsequently. It is even possible to take away some of the remaining lung tissue. The difficulty of the operation lies mainly in dealing with the stump of the main bronchus. The remaining lung undergoes a compensatory enlargement whose maximum is reached in thirty to sixty days. The empty pleural cavity on the side of extirpation is gradually filled in by a displacement of the heart and mediastinum, while the diaphragm rises considerably and the thoracic wall becomes depressed upon the side of operation. In some instances spinal curvature with its convexity toward the side of the operation develops. There are no histological changes of any note in the thoracic tissues, save evidence of compensatory emphysema with more or less hypertrophy of the pulmonary tissues.

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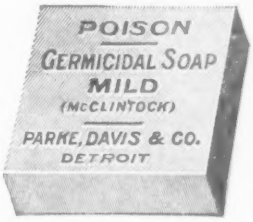

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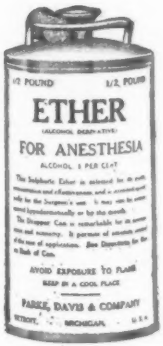

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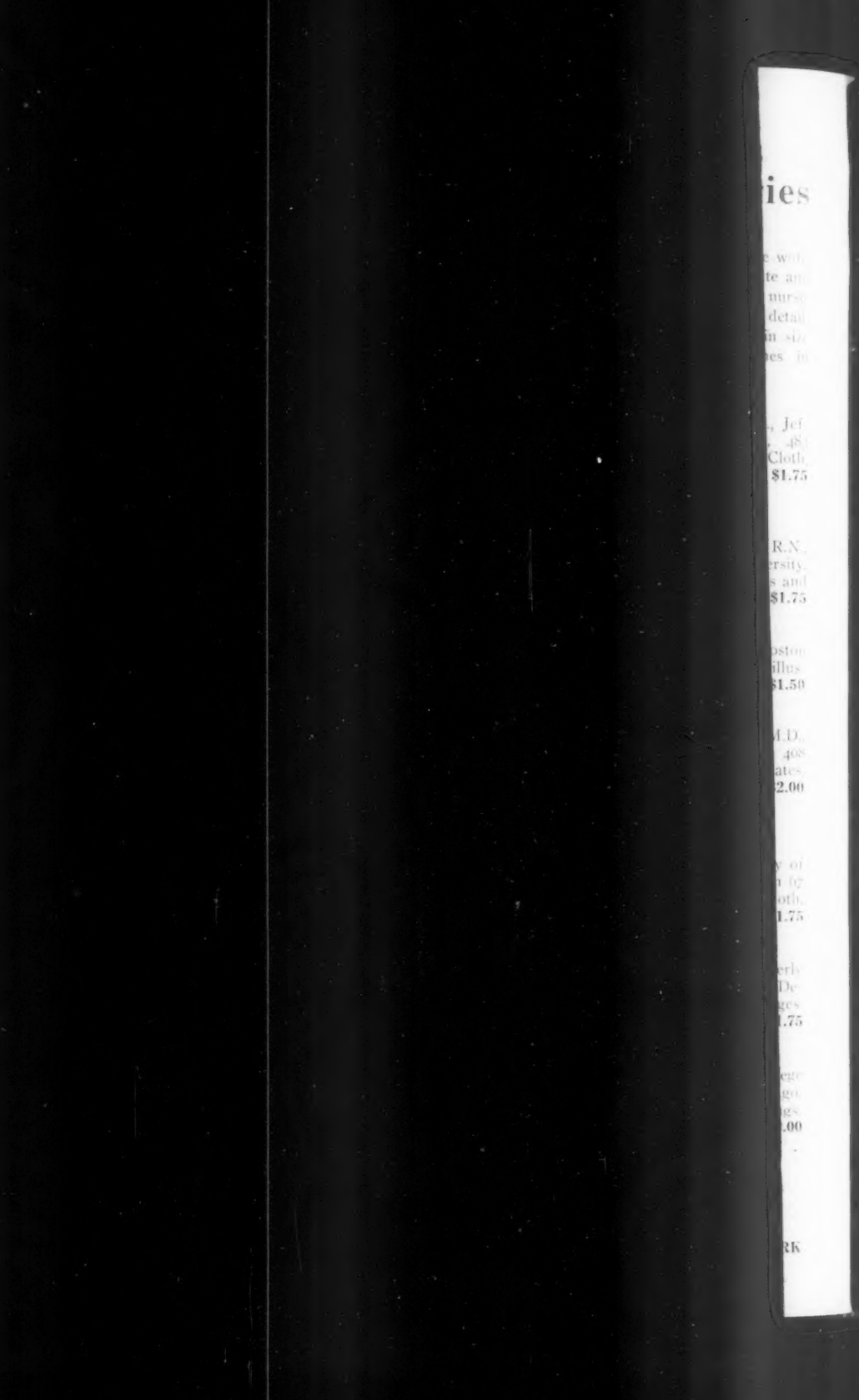

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